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Pathology

EXPERIMENTAL PATHOLOGY

1123. **Visceral and Plasma Changes in Cholesterol-fed Rabbits with Raised Blood-pressure**
R. H. HEPTINSTALL and B. BRONTE-STEWART. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **68**, 395–405, 1954. 10 figs., 12 refs.

The authors, working at St. Mary's Hospital, London, have studied the visceral changes and the changes in the plasma cholesterol level caused by feeding cholesterol to groups of rabbits. Hypertension was induced in one group by unilateral nephrectomy and the application of a silver clip to the other renal artery; no operation was performed on a second group of animals. Each of these groups was divided into two sub-groups, one of which was given cholesterol for 72 days, the other an identical diet but no cholesterol.

In both groups of cholesterol-fed rabbits the plasma cholesterol level rose rapidly for 6 weeks, after which it rose less steeply and in some cases actually fell. Considerable lipid infiltration of the liver, adrenal glands, spleen, and kidneys was observed in these animals. The small intramuscular branches of the coronary arteries showed a diffuse intimal infiltration with lipid and considerable reduction of the lumen. The severity of these lesions bore no relation to the extent of the aortic atheroma. In the aorta the severest lesions were found in the arch, the intima being infiltrated with lipid-laden macrophages, often many layers deep, so that in some plates the intima was 600 μ thick. [For further details see Abstract 1124.] Pulmonary atheroma was comparable in both cholesterol-fed groups.

The authors have established that although the rabbit is a herbivorous animal it is able to deal quite adequately with moderate amounts of cholesterol. *E. G. Rees*

1124. **The Relationship between Experimental Hypertension and Cholesterol-induced Atheroma in Rabbits**
B. BRONTE-STEWART and R. H. HEPTINSTALL. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **68**, 407–417, 1954. 3 figs., 15 refs.

The investigation described in this paper was undertaken to determine whether raising the blood pressure accentuates the amount of atheroma produced by cholesterol feeding in rabbits. The authors have shown that hypertension appears to accelerate the onset and to increase the severity of atheroma in the aorta. This effect is noticed only in the systemic circulation and cannot be attributed to local turbulence from aortic constriction. It would appear that the rise in pressure need not be of long duration to accentuate atheroma formation, and there is a closer correlation of the extent of the aortic atheroma with the variability of the blood pressure as estimated from day to day than with the mean blood pressure itself.

In the absence of cholesterol feeding constriction of the renal artery to the sole remaining kidney did not result in aortic atheroma or a rise in the plasma cholesterol level. Cholesterol feeding for 10 weeks led to a slight but significant rise in blood pressure during the last few weeks of this period. The mechanism of this rise was not apparent. *E. G. Rees*

1125. **Distribution of Acid Mucopolysaccharides and Lipids in Tissues of Cholesterol-fed Rabbits**
R. C. BUCK. *Archives of Pathology* [*Arch. Path. (Chicago)*] **58**, 576–587, Dec., 1954. 7 figs., 24 refs.

CHEMICAL PATHOLOGY

1126. **The Clinical Significance of Serum Aldolase**
J. A. SIBLEY and G. A. FLEISHER. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **29**, 591–603, Nov. 10, 1954. 7 figs., 8 refs.

Aldolase is an enzyme which plays an important part in the chain of reactions resulting in glycolysis. Its action is specific, consisting in the reversible splitting of 1 mol of fructose diphosphate into 2 mols of triose. It was reported by Warburg and Christian (*Biochem. Z.*, 1943, **314**, 399) that 5 of the 11 enzymes concerned in glycolysis were present in the blood serum of rats and that the levels of two of these, aldolase and triose isomerase, were consistently increased above normal in the serum of rats bearing large tumours. These observations were confirmed by Sibley and Lehninger, but they found a significant increase in serum aldolase level in only about 20% of human subjects with malignant disease (*J. biol. Chem.*, 1949, **177**, 859; *J. nat. Cancer Inst.*, 1949, **9**, 303). Other workers, however, have reported that the serum aldolase level is consistently increased in various diseases, such as carcinoma of the prostate, myopathies, and acute hepatitis. The present investigation was therefore undertaken in order to determine the diagnostic value, if any, of the test, and involved the estimation of the serum aldolase content of 1,200 blood samples from 880 persons, most of whom were patients under treatment at the Mayo Clinic for a

variety of diseases. All determinations were carried out by the colorimetric method described by Sibley and Lehninger, one unit of aldolase activity being defined as the amount necessary to split the fructose diphosphate contained in 1 c.mm. of a 0·025 M solution in 1 hour under the conditions of the test. The average serum aldolase level in 115 normal subjects was 6 units per ml. with a range of 3 to 10 units per ml. The individual values were not related to age or sex.

Essentially normal serum aldolase values were found in the majority of cases of acute and chronic inflammatory disease of many types and in postoperative states, in cardiovascular disease and metabolic and endocrine disorders of many varieties, in non-malignant blood dyscrasias, and in uraemia. An increase in the serum aldolase level was noted in only 2 of 5 patients with myopathies (including polymyositis, dermatomyositis, and progressive muscular atrophy), and normal values were found in all cases of secondary muscular atrophy, as in amyotrophic lateral sclerosis and polyneuritis. A definite increase was frequently found in acute haemorrhagic pancreatitis, severe haemolytic anaemia (mainly erythroblastosis foetalis), and acute alcoholic psychosis. A study of 219 patients with hepatic disease showed a great increase in the serum aldolase level, up to 10 times the average normal values, in all cases of early acute hepatitis, but the value was normal or only slightly increased in patients with obstructive jaundice or cirrhosis of various types. The level in acute hepatitis was not related to the status of hepatic function or degree of retention of bile; the level increased very early in the course of the disease and, in mild cases, soon returned to normal. It is concluded that the increase in serum aldolase level in acute hepatitis is of sufficient magnitude and specificity to be of value in differential diagnosis. A significantly increased value was found in 23% of 168 cases of various malignant diseases, but was without relation to type, site, or extent, except that in cases of leukaemia a high serum aldolase level was always associated with a high leucocyte count and vice versa.

The mechanism producing an increase in serum aldolase level must be totally unlike that which accounts for an increase in serum alkaline-phosphatase level, since the former was normal in cases of obstructive jaundice in which the latter was greatly increased. A feature common to all cases in which an excess of aldolase was found in the serum was acute and extensive destruction of tissue, and it is suggested that the excess was due to the release of this intracellular enzyme from damaged cells, the aldolase normally present being accounted for by physiological breakdown of cells. *E. Forrai*

1127. **Free Erythrocyte Porphyrin and Plasma Copper in Rheumatoid Disease.** [In English]
M. R. Jeffrey and D. Watson. *Acta haematologica* [*Acta haemat. (Basel)*] **12**, 169–176, Sept., 1954. 2 figs., 14 refs.

The anaemia of rheumatoid arthritis is similar in many respects to the anaemia of sepsis. As it has been shown that in the latter the concentration of free erythrocyte protoporphyrin and serum copper is raised, the authors, in a study here reported from the Royal National Hospital for Rheumatic Diseases, Bath, determined the levels of these substances in the heparinized venous blood of fasting control subjects and patients with rheumatoid arthritis, using for the former determination the method of Grinstein and Watson (*J. biol. Chem.*, 1943, **147**, 675) and for the latter the method of Watson. The plasma iron content was also estimated.

In 20 normal subjects the mean value of free erythrocyte porphyrin (essentially protoporphyrin) was 21·5 μg. (maximum 44 μg.) per 100 ml. of erythrocytes. In uncomplicated cases of rheumatoid arthritis (excluding those with conditions producing iron deficiency) this value was within the upper limit of normal (taken as 60 μg. per 100 ml.) in two-thirds of the cases, but was above it in 9 out of 20 men, and in 5 out of 30 women. There was a high negative correlation with haemoglobin value ($r = -0{\cdot}49$) and with plasma iron content ($r = -0{\cdot}68$ in men, $-0{\cdot}46$ in women), but no significant correlation with age or with duration or activity of the illness. After treatment with iron (given intravenously as saccharated iron oxide 3 times weekly for 3 months) the porphyrin value, where it had been abnormally high, returned to within normal limits.

The average plasma copper concentration was 101 μg. per 100 ml. for 20 normal men and 106 μg. for 20 normal women, the upper limits of normal being taken as 120 and 135 μg. per 100 ml. respectively. Of the patients with rheumatoid arthritis, 25 out of 35 men and 52 out of 65 women gave results above the normal range, with means of 144 μg. and 159 μg. per 100 ml. respectively. There was a negative correlation between plasma copper levels and haemoglobin values ($r = -0{\cdot}70$ and $-0{\cdot}55$ for men and women respectively), and also between plasma iron concentration and copper content ($r = -0{\cdot}76$ and $-0{\cdot}54$ respectively). After treatment with gold salts (given intramuscularly as calcium aurothiomalate over about 5 months to a total of 1 g. of the metal), plasma copper values did not change significantly in 18 cases despite a mean rise in the haemoglobin value of 1 g. per 100 ml.; in response to intravenous iron therapy, high copper levels increased somewhat and remained high despite correction of the anaemia. The authors conclude that the raised porphyrin values observed were due to iron deficiency rather than to the rheumatoid arthritis; but the hypercupraemia observed is only partly explained by the presence of anaemia and could, they suggest, be due to decreased utilization of copper in consequence of the impaired formation of haemoglobin and erythrocytes thought to be present in rheumatoid anaemia.

E. G. L. Bywaters

1128. **The Dye-binding Capacity of Human Plasma Determined Fluorimetrically and Its Relation to the Determination of Plasma Albumin**
V. H. Rees, J. E. Fildes, and D. J. R. Laurence. *Journal of Clinical Pathology* [*J. clin. Path.*] 7, 336–340, Nov., 1954. 3 figs., 12 refs.

The binding of acidic dyes by the plasma proteins is a specific property of the albumin fractions; for example, if bromophenol blue is added to plasma which is then subjected to electrophoresis on filter paper, the blue dye migrates solely with the plasma albumin. In the work

reported in the present paper from the Postgraduate Medical School of London the use of the acidic dye 1-anilino-naphthalene-8-sulphonic acid for the estimation of the albumin content of plasma was investigated. This substance is non-fluorescent in aqueous solution but brightly fluorescent when absorbed by plasma albumin, so that the fluorescent intensity of a mixture of dye and plasma (dye-binding capacity of the plasma) should provide a measure of the plasma albumin content.

The procedure consisted briefly in mixing 0·05 ml. of plasma with 7 ml. of a solution prepared by adding 2 mg. of the dye (dissolved in 0·1 N caustic soda and diluted to 250 ml. with water) to 50 ml. of a phosphate buffer and 50 ml. of normal saline, the fluorescence then being measured in a fluorimeter in arbitrary units. The plasma albumin concentration was then read off from a standard curve previously constructed from standard solutions of human plasma albumin. The results were compared with those obtained by four other methods: (1) salt fractionation with sodium sulphite; (2) electrophoresis on filter paper using a commercial densitometer; (3) electrophoresis on filter paper using a recording densitometer; (4) electrophoresis on filter paper with elution and subsequent colorimetric estimation of the dyed bonds.

The dye-binding capacity of the plasma in a random selection of pathological conditions, including nephritis and nephrosis, bore a close, almost linear, relationship to its albumin content. However, consistently low values of dye-binding capacity were obtained in cases of obstructive and hepatic jaundice, and it was considered possible that the bile pigments present may have interfered with the measurement of the fluorescence. There was good agreement between the values obtained by measurement of the dye-binding capacity and by Methods 3 and 4, but Method 1 gave a wide scatter of results and the use of Method 2 resulted in underestimation of the plasma albumin content.

[The original paper should be consulted for the technical details of fluorimetry and the preparation of the dye.] *M. J. H. Smith*

1129. **The Estimation of Heparin and Similar Substances in Human Blood and Tissues Using a Combined Biological and Colorimetric Method with Paper Electrophoretic Studies**

M. Bassiouni. *Journal of Clinical Pathology* [*J. clin. Path.*] **7**, 330–335, Nov., 1954. 6 figs., 7 refs.

1130. **Evaluation of Provocative Blood Enzyme Tests Employed in Diagnosis of Pancreatic Disease**

D. A. Dreiling and A. Richman. *Archives of Internal Medicine* [*Arch. intern. Med.*] **94**, 197–212, Aug., 1954. 1 fig., bibliography.

After a brief consideration of the various tests which have been devised for the detection of pancreatic dysfunction, followed by a rapid review of the literature, the authors present a series of studies in which provocative tests designed to raise the blood amylase level were performed at Mount Sinai Hospital, New York, on 192 patients with and without proved pancreatic disease. The blood amylase level was determined before and at 1, 2, and 3 hours after administration of the provocative stimulus, which consisted of secretin (100 clinical units intravenously), morphine (15 mg. subcutaneously), methacholine (20 mg. subcutaneously), or bethanechol (5 mg. subcutaneously), these substances being given either singly or in combination. In a few cases shorter time intervals elapsed between the determinations.

These 4 drugs given singly caused a significant rise in blood amylase level in 0 out of 18, 2 out of 17, 4 out of 16, and 3 out of 12 patients without pancreatic disease respectively, and in 1 out of 15, 2 out of 10, 4 out of 15, and 3 out of 10 patients with pancreatic disease. The combination of secretin and morphine, secretin and methacholine, and secretin, methacholine, and morphine caused a significant rise in blood amylase values in 1 out of 17, 0 out of 15, and 7 out of 14 control subjects and in 4 out of 13, 2 out of 11, and 3 out of 12 patients with pancreatic disease respectively. The authors conclude that the wide variability of the response to these provocative stimuli renders them useless for the diagnosis of pancreatic disease. *A. C. Frazer*

1131. **The Effect of the Previous Diet on Glucose Tolerance Tests**

E. M. Irving and I. Wang. *Glasgow Medical Journal* [*Glasg. med. J.*] **35**, 275–278, Nov., 1954. 7 refs.

The soundness of Conn's suggestion (*Amer. J. med. Sci.*, 1940, **199**, 555) that for 3 days before a glucose tolerance test the patient should take a diet containing at least 300 g. of carbohydrate has been examined at the Victoria Infirmary, Glasgow. In 7 healthy males and 5 healthy females the effect on the glucose tolerance curve of a diet containing 100 g. daily of carbohydrate, which was considered to be less than the normal consumption of a hospital patient of adequate nutrition, was compared with that of a diet containing 300 g. daily. The differences between the two curves were insignificant, although in 2 cases an oxyhyperglycaemic ("lag") curve was obtained after the low-carbohydrate diet. It is concluded that the normal diet of an adequately nourished patient need not be augmented before a glucose tolerance test is carried out. *J. E. Page*

1132. **The Rate of Absorption of Phenolsulphonphthalein Injected Intraperitoneally as a Test of Progress in Alcoholic Cirrhosis with Ascites.** (L'épreuve de l'élimination de la phénol-sulfone-phtaléine injectée par voie intra-péritonéale comme test évolutif des cirrhoses alcooliques ascitiques)

Y. Boquien, G. Alliot, and —. Sigogneau. *Presse médicale* [*Presse méd.*] **62**, 1496–1499, Nov. 3, 1954. 7 figs.

While studying the disturbance of protein balance in alcoholic cirrhosis of the liver at the Nantes Faculty of Medicine, the authors investigated the possibility of estimating the volume of ascitic fluid present in such cases by the intraperitoneal injection of phenolsulphonphthalein (phenol red), which was chosen because of its rapid diffusion through the fluid, and the subsequent colorimetric determination of its concentration in the

fluid. It was found incidentally that there were great differences between individuals in the rate of disappearance of the dye from the peritoneal fluid, although in any one subject the rate remained virtually constant, the graph showing concentration as a function of time after injection being a straight line. It was also found that the rate of elimination in each subject was correlated sufficiently closely with the clinical state and the prognosis for its determination to be of clinical value.

In the procedure adopted 12 ml. of a 0·15% solution of phenol red is injected intraperitoneally, after which the patient is made to move about in order to ensure the even distribution of the dye. After 5 minutes a sample of fluid is taken, from which the volume of ascitic fluid present may be determined. If there is any reason to suspect uneven diffusion of the dye, samples are taken simultaneously from the two sides of the abdomen and their dye content compared. Further samples are taken 1, 3, and 5 hours after the injection and an elimination curve constructed from which the time for total elimination may be determined by extrapolation.

The test was performed on 20 patients suffering from cirrhosis of the liver with ascites, 15 of whom had hypertrophic and 5 atrophic cirrhosis. In 19 cases the cirrhosis was of alcoholic origin, and in one it was due to cinchophen poisoning. In all cases the results of standard tests showed a marked disturbance of liver function. Of the 10 patients in whom the elimination of the test dose of phenol red was prolonged beyond 8 hours, 6 have since died and the remaining 4 are in a stationary condition, whereas of the 10 in whom elimination was complete in less than 8 hours, all except one (who died from peritonitis 1½ months after the test was carried out) have improved.

The various factors affecting the speed of elimination of phenol red from ascitic fluid are discussed and it is concluded that the result of the test is determined principally by the state of the portal circulation, although it will certainly be affected by other factors—particularly by the development of a portacaval shunt. *E. Forrai*

1133. **Clinical Use of the Urinary Uropepsin Determination in Medicine and Surgery**
S. J. GRAY, C. G. RAMSEY, and R. W. REIFENSTEIN. *New England Journal of Medicine* [*New Engl. J. Med.*] **251**, 835–843, Nov. 18, 1954. 2 figs., 23 refs.

The urinary excretion of uropepsin in various gastrointestinal and endocrine disorders and in patients subjected to gastric resection, total gastrectomy, or vagotomy was studied at Peter Bent Brigham Hospital, Boston. [For details of the method of estimating the urinary uropepsin content the original paper should be consulted.]

It was found that the urinary excretion of uropepsin was high in patients with duodenal ulcer—8,762 units in 24 hours compared with the normal of 2,300 units in 24 hours. In patients with gastric ulcer the 24-hour excretion was significantly lower than that in patients with duodenal ulcer but was well above normal, while in patients with gastric carcinoma the 24-hour excretion was only 980 units. Generally, a low urinary excretion of uropepsin was associated with diminished gastric acidity and a high urinary excretion with increased gastric acidity. The value of these findings in the differential diagnosis of gastrointestinal disease is discussed. It was also found that a high output of uropepsin accompanied increased adrenocortical activity and a low output accompanied adrenal hypofunction. Vagotomy did not appear to affect the output or the uropepsin response to adrenocortical stimulation.

It is concluded that these findings support the view that acute and chronic stress stimulate the stomach by way of a humoral mechanism which is independent of the vagus nerve. *J. B. Wilson*

1134. **The "Total Urinary Clearance" (C_Σ) of the Healthy Kidney under Various Conditions and its Relation to Renal Water Metabolism.** (Die "Clearance der Harnfixasumme" (C_Σ) unter verschiedenen Absonderungsarten der gesunden Nieren und ihre Beziehungen zur renalen Wasserbearbeitung)
J. FREY, J. SCHIRMEISTER, and H. HENNING. *Archiv für experimentelle Pathologie und Pharmakologie* [*Arch. exp. Path. Pharmak.*] **223**, 107–116, 1954. 6 figs., 13 refs.

The estimation of total urinary clearance (C_Σ) (Frey, *Urologia*, 1952, **6**, 461) permits the accurate differentiation of two independent types of renal function—filtration and water excretion. In filtration diuresis C_Σ rises steadily with the rate of urinary flow, mainly as a result of the increase in sodium chloride excretion, whereas in water diuresis there is an upper limit ("augmentation limit") of 2·5 ml. per minute above which C_Σ does not rise, even though the urinary flow may continue to increase. Theoretical considerations lead to the conclusion that the difference (T_{H_2O}) between C_Σ and urinary flow per minute is equal to the volume of water absorbed or excreted by the tubules to give the ultimate concentration of the urine. It thus appears—in the case of moderate filtration diuresis—that with a total urinary clearance of 2·5 ml. per minute and a urinary flow of 1·0 ml. per minute, 1·5 ml. of water is reabsorbed by the tubules per minute; with C_Σ unchanged and a urinary flow of 3·0 ml. per minute excretion of water by the tubules is at the rate of 0·5 ml. per minute, and with a urinary flow of 10 ml. per minute tubular excretion of water amounts to 7·5 ml. per minute. *L. H. Worth*

1135. **The Renal Excretion of Water after Increased Water Intake (Water Diuresis).** (Die renale Wasserausscheidung bei oraler Aufnahme grösserer Wassermengen (Wasserdiurese))
J. FREY and J. SCHIRMEISTER. *Archiv für experimentelle Pathologie und Pharmakologie* [*Arch. exp. Path. Pharmak.*] **223**, 117–121, 1954. 2 figs., 13 refs.

Experiments on human subjects and on mice are described from which it is concluded that in healthy individuals the increased output of urine after the intake of large amounts of water (more than 3 litres in as short a time as possible) is mainly due to filtration diuresis, with increased excretion of sodium chloride. It is also postulated that tubular excretion of water plays a more important part in the diuresis which follows the intake

of water than has hitherto been accepted. Platt's conception of the mechanism of diuresis is based on this assumption, and is supported by the present authors.

L. H. Worth

1136. **Peculiarities of Filtration Diuresis.** (Über Besonderheiten der Filtrationsdiurese)
J. Frey and J. Schirmeister. *Archiv für experimentelle Pathologie und Pharmakologie* [*Arch. exp. Path. Pharmak.*] **223**, 122–126, 1954. 2 figs., 16 refs.

The close examination of graphs recording the changes in total urinary clearance and in rate of urinary flow which occur during filtration diuresis resulting from the administration of caffeine and mercurial diureties shows that at a certain point, when urinary flow is in the medium range, a change occurs in the pattern of renal function, indicating that additional factors, such as water diuresis and antidiuretic influences, come into play. It is suggested that the reduction of plasma electrolyte concentration resulting from forced filtration diuresis stimulates the secretion of vasopressin by the pituitary gland.

L. H. Worth

HAEMATOLOGY

1137. **Further Research on Haematopoietin.** (Nouvelles recherches sur l'hématopoiétine)
P. Gley. *Bulletin de l'Académie nationale de médecine* [*Bull. Acad. nat. Méd. (Paris)*] **138**, 435–440, Oct. 19, 1954. 2 figs., 11 refs.

Further work is reported on " haematopoietin ", the haematopoietic hormone which is alleged to appear in the blood after repeated bleedings (Gley, *Bull. Acad. nat. Méd.* (*Paris*), 1952, **116**, 521; *Abstracts of World Medicine*, 1953, **13**, 267). The origin of this hormone appears to vary in different animals. The ordinary reticulocytosis that follows bleeding fails to appear after thymectomy, but it is not suggested that the thymus gland is the only site of formation of the hormone—indeed, some evidence is adduced that the pituitary gland controls its formation, at least in rabbits, guinea-pigs, and monkeys.

Haematopoietin has been isolated and crystallized, but its exact nature is still being investigated. It is never present in large amounts, its usual concentration being less than 0·1 mg. per litre, which accounts for the difficulty of its isolation. It is claimed that haematopoietin is a lipid hormone which acts directly on the bone marrow and stimulates the production of pro-erythrocytes.

A. Piney

1138. **Clinical Application of Simplified Serum Prothrombin Consumption Test**
L. N. Sussman, I. B. Cohen, and R. Gittler. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **156**, 702–705, Oct. 16, 1954. 4 figs., 11 refs.

The authors discuss the significance of the serum prothrombin consumption test and describe in detail a simplified method in use at the Beth Israel Hospital, New York. They emphasize the fact that careful attention must be paid to the details of technique as minor variations, particularly, for example, in the duration of incubation, may produce very marked differences in the results. The essentials of the method are as follows. Thromboplastin solution is prepared as for the plasma prothrombin test, and a fibrinogen solution containing 300 mg. of fibrinogen per 100 ml. of 85% sodium chloride solution is made up. Just before the test 2 ml. of the former is mixed with 1 ml. of the latter. To 0·2 ml. of this mixture is added 0·1 ml. of the serum to be tested, both having been kept at 37° C. for 5 minutes, and the time for the clot to form, which it does as a fine web, is observed. Clotting times longer than 30 seconds are interpreted as normal, times shorter than 20 seconds as abnormal, and times between as doubtful.

In normal coagulation the presence of excess thromboplastin complex leads to almost complete consumption of prothrombin. The thromboplastin complex represents the activity of several factors, including extracts from the breakdown of platelets and tissue and certain plasma fractions, for example, antihaemophilic globulin, plasma thromboplastin component, and plasma thromboplastin antecedent. Therefore any defect in one of these factors will result in decreased utilization of prothrombin.

The serum prothrombin time as determined by the authors' method in several hundred normal persons was longer than 25 seconds; the mean results in 250 patients with various pathological conditions are tabulated. Abnormal serum prothrombin times were found in patients with thrombasthenia, acute myeloid leukaemia, thrombocytopenic purpura, haemophilia, aplastic anaemia, secondary thrombopenia, and after splenectomy. All these conditions are associated with a defect in the thromboplastin complex. The authors emphasize the usefulness of the test in the detection of defects in the functional activity of platelets. They conclude that although further investigation of the method in varied clinical conditions and of the effect of certain drugs on blood coagulation is required, the test is of value in the investigation of coagulation defects.

R. F. Jennison

1139. **The Appearance and Significance of Tissue Mast Cells in Human Bone Marrow**
J. M. Johnstone. *Journal of Clinical Pathology* [*J. clin. Path.*] **7**, 275–280, Nov., 1954. 3 figs., 32 refs.

The author reports, from the University and Western Infirmary, Glasgow, a study of the incidence of tissue mast cells in human bone marrow, and assesses their possible significance. In an examination of 269 fixed tissue sections of marrow aspirates (mostly from the sternum) of 230 patients no such cells were found in the marrow of 68 patients (30%), up to 5 mast cells in each microscopical field in 139 cases (60%), and over 5 in each field in 23 (10%). Of 27 cases in which more than one specimen was obtained from the same patient, a closely similar distribution was noted on each occasion in 21 cases. Mast cells were rarely and scantily found in children. No correlation was apparent between the number of mast cells and the iron content of the marrow or degree of erythropoiesis.

Mast cells were found in a wide variety of pathological conditions, and these are tabulated. In only 2 of the 23 cases showing mast-cell accumulation was there hypo-

plasia of the marrow, the marrow in all others being normal or hyperplastic; out of 16 cases of hypoplasia only 5 showed mast-cell accumulation. In view of the reported finding that mast cells contain heparin and histamine a correlation with a chronic inflammatory or allergic state was sought, but was not found. Anaemia and splenomegaly were commonly, but not invariably, associated with an increase in the number of mast cells. The author considers the possibility that adrenal cortical hypofunction may be responsible for mast-cell proliferation when the marrow is hypoplastic, but this has not been confirmed experimentally.

It is concluded that mast cells are a normal constituent of human bone marrow and that the former belief that their presence is of gloomy prognostic significance cannot be substantiated. *Marjorie Le Vay*

1140. **Atypical Giant Cells in the Spleen of Leukemic Conditions.** [In English]
E. SCHWARZ. *Acta medica Scandinavica* [*Acta med. scand.*] **150**, 119–130, Oct. 2, 1954. 18 figs., 24 refs.

During the course of an investigation of extramedullary megakaryocytosis, carried out at the Medical Research Institute and Michael Rees Hospital, Chicago, the author encountered large, conspicuous cells of another type in the spleen of patients with acute myeloid leukaemia. This cell, which does not seem to have been previously described, is best seen with Giemsa stain or haematoxylin. It is a large cell, about 25 μ in diameter, with metachromatic, intensely basophilic cytoplasm, a large, vesicular, lobed nucleus, and enormous nucleoli. It is confined to the lymphatic structures, particularly the Malpighian bodies, occurs singly, and is usually surrounded by a reticular reaction. Morphologically, and also in distribution, it appears to be associated with plasma cells, and is considered to be probably the result of a reticular reaction to a particular stimulus. The cells bore no relation to the surrounding lymphocytes. The appearance of the cell is portrayed in a number of photomicrographs. *Marjorie Le Vay*

MORBID ANATOMY AND CYTOLOGY

1141. **Brain Changes in Patients with Extensive Body Burns**
L. MADOW and B. J. ALPERS. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] 72, 440–451, Oct., 1954. 4 figs., 16 refs.

Approximately 8,000 deaths from burns occur in the United States each year. Although cerebral changes have been described in patients with very severe burns about the body, few detailed neuropathological investigations have been reported. In this paper from Jefferson Medical College, Philadelphia, the neuropathological features in 2 cases of extensive body burns are described.

The first patient, a boy aged 14 years, had 3rd-degree burns over 40% of the body surface. He became irrational on the 7th day; anuria, stupor, and pyrexia supervened and he died on the 16th day. At necropsy the brain showed toxic ganglion-cell changes, small fresh haemorrhages in the white matter, and focal areas of demyelination with very little glial proliferation. The second patient, a man aged 35 years, had 3rd-degree burns over 95% of the body surface. On the 10th day he became comatose; he died on the 12th day. Examination of the brain at necropsy revealed meningitis and subarachnoid haemorrhage, as well as toxic ganglion-cell changes, haemorrhages within the brain substance, and small areas of demyelination.

The neuropathological findings in these 2 cases appeared to fall into three main groups: (1) cerebral oedema and blood-vessel changes; (2) ganglion-cell changes; and (3) changes in the axis cylinders and myelin. Macroscopically, cerebral oedema appeared as patches of swollen gyri and obliterated sulci. Microscopically, perivascular spaces were dilated, with marked engorgement of the blood vessels in the parenchyma. In the white matter there were small, ring-like haemorrhages around a smaller cuff of glial cells, which in turn surrounded blood vessels with swollen or broken down endothelium (" brain purpura "). The ganglion-cell changes were of the toxic type. Most of the cells were swollen, with loss of much of the Nissl substance, and had either eccentric or extruded nuclei. Glial proliferation (prominent only in the second case) was mainly astrocytic, with neuronophagia. In the myelin the two predominant features were a swelling of the myelin sheath without cellular reaction, mainly around blood vessels, and focal destruction of myelin and axis cylinders.

These changes suggest a toxic rather than an anoxic effect on the central nervous system. Some of them were irreversible and, in the authors' view, might give rise to convulsions, mental deterioration, or a postencephalitic type of clinical picture. *Adrian V. Adams*

1142. **Subendocardial Haemorrhages Associated with Intracranial Lesions**
R. P. SMITH and B. E. TOMLINSON. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **68**, 327–334, 1954. 6 figs., 12 refs.

The authors, writing from the General Hospital, Newcastle upon Tyne, describe the finding of subendocardial haemorrhages, usually small, in the left ventricle of the heart in 29 out of 235 patients in whom death was due primarily to an intracranial lesion. The haemorrhages occurred most commonly in the interventricular septum and were very superficially placed; only in one instance was coagulative necrosis of muscle noted and then it was confined to a few superficial fibres. Gastric mucosal haemorrhages were observed in 31 cases, and in all but 4 of these the accompanying intracranial lesions resembled those associated with the cardiac haemorrhages. In only 11 of the 31 cases were there cardiac as well as gastric haemorrhages. Cardiac haemorrhages were found in association with most of the common types of intracranial lesion; however, they were seen most frequently only when there had been a sudden rise in intracranial pressure. It is suggested that cardiac haemorrhage in these cases was due to systemic hypertension following temporary cardiac arrest from vagal inhibition. No correlation was found between the incidence of cardiac

haemorrhages and the age of the patient or the presence of pulmonary lesions such as congestion, oedema, haemorrhage, and bronchopneumonia.

A. Wynn Williams

1143. **Nephrosis and Fat Embolism in Acute Hemorrhagic Pancreatitis**

M. J. LYNCH. *Archives of Internal Medicine* [*Arch. intern. Med.*] **94**, 709–717, Nov., 1954. 9 figs., 5 refs.

At the General Hospital, Sudbury, Ontario, 6 cases of pancreatitis were studied post mortem from the point of view of renal involvement. In 5 of the cases the disease was of the acute haemorrhagic type and the renal appearances were of pronounced nephrosis with intense epithelial damage in the convoluted tubules. Histological examination of frozen sections showed fat emboli in the capillaries of the glomerular tufts and in the efferent and intertubular arterioles and capillaries. Fat droplets were also present in the lumina of the tubules and there were large fat vacuoles in the epithelial cells. The sixth case—one of chronic pancreatitis, the acute phase being thought to have occurred from 2 to 9 months before death—showed a chronic renal lesion. There was a great increase in interstitial connective tissue, with severe reduction in the number of the convoluted tubules. The glomeruli showed a general reduction in size, a diminished number of capillary tufts, and an increase in the intercapillary ground substance. A striking feature was the presence of calcium deposits throughout the kidneys just outside the tubular basement membranes and between the closely-set tubules.

The author concludes that the chief connecting link between acute necrotizing pancreatitis and nephrosis is the occurrence of fat embolism, the degree of ischaemic nephrosis being directly proportional to the degree of fat embolization. He considers it possible, however, that circulating enzymes and toxic products from the tissues may also contribute to the renal condition. It was unfortunately not possible in these cases to examine the brain for evidence of fat embolism. *R. B. Lucas*

1144. **The Pathology of Regional (Segmental) Colitis**

H. W. NEUMAN and M. B. DOCKERTY. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **99**, 572–579, Nov., 1954. 8 figs., 11 refs.

Localized ulcerative disease involving the colon but not the rectum or rectosigmoid has been described under various names since the beginning of the century. In 1945 Barbosa *et al* (*Surg. Clin. N. Amer.*, 1945, **25**, 939) described 140 cases of this condition, which they termed regional (segmental) colitis. The present authors describe the pathological features of the disease as observed in 25 specimens of tissue removed at operation from the involved segment of the intestine. Macroscopically the length of colon involved varied greatly and the tendency was for the disease to spread towards the rectum, although in 7 instances the terminal ileum was involved. Longitudinal shortening was consistently present, but not always constriction, while the degree of thickening of the colonic wall varied within each specimen. Excessive amounts of fat surrounded the diseased portion of the colon. Ulceration of the mucous membrane was observed in 17 specimens; this was noted microscopically in 20. The ulcers were usually diffusely distributed, of varying sizes, shallow with no undermining of the edge, and linear and ovoid in shape. In some areas the intervening mucosa was thin and smooth; in others it was hyperplastic. Polypoid hyperplasia was seen in 14 of the specimens. The change from diseased to normal intestine was sharp, no abnormality being found microscopically 6 cm. beyond the gross limits of the lesion.

Microscopically, the ulceration of the mucous membrane extended for varying distances into the submucosa. The ulcer bases were surrounded by broad or narrow zones of acute or subacute inflammatory cells, beneath which were areas of granulation tissue heavily infiltrated with chronic inflammatory cellular elements. Abscesses, haemorrhage, and, in one case, giant cells and granuloma formation were seen adjacent to the areas of ulceration. In the intervening mucosa oedema, diffuse infiltration largely with plasma and epithelioid cells and a few polymorphonuclear leucocytes, and, in 6 instances, an acute purulent cryptitis were observed. There were no malignant changes. The muscularis mucosae was disorganized, the muscle bundles being either separated by oedema or fibrosis or completely destroyed. In the submucosa propria and muscularis propria there were diffuse cellular infiltrations, largely with plasma and epithelioid cells and lymphocytes, non-caseating giant-cell systems, and frequently lymphoid hyperplasia. Mesenteric lymphadenopathy was not marked, but focal granulomata were occasionally seen in the lymph nodes.

The authors suggest that the earliest pathological lesion in the intestine may be the purulent cryptitis, which is followed by abscess formation and ulceration of the overlying mucosa. *A. Ackroyd*

1145. **Reticulohistiocytic Granuloma ("Reticulohistiocytoma") of the Skin**

W. E. PURVIS and E. B. HELWIG. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **24**, 1005–1015, Sept., 1954. 14 figs., 7 refs.

Reticulohistiocytoma cutis is a rare condition and its striking histological appearance may give rise to great diagnostic difficulties for those unfamiliar with it. The 44 cases collected from the files of the Armed Forces Institute of Pathology, Washington, D.C., which are reported here constitute the first substantial series to be published.

Clinically, the lesion consists of a nodule in the skin up to 20 mm. in diameter, but without diagnostic features: there are often multiple nodules (7 out of 44 cases) and the preferred site is the head and neck (20 out of 44). Of 27 patients who were followed up over periods ranging from 2 months to 11 years, 2 had had a local recurrence and 3 had developed nodules at another site. Histologically, the nodule lies superficially in the dermis, usually immediately below, but not involving, the epidermis. The characteristic feature is the presence of many large giant cells with multiple, large, irregular nuclei, often with prominent nucleoli, and frequently

containing iron and fat. There are present in addition many histiocytes, inflammatory cells, and stromal spindle cells. The presence both of giant cells and of the histiocytic and inflammatory elements is probably essential for diagnosis. Foreign-body cells or Touton giant cells are common, and the authors claim to have demonstrated an apparent transition from the histiocyte to the characteristic giant cell. They regard these lesions as reactive rather than neoplastic. *Bernard Lennox*

1146. **Solitary Mast-cell Naevus**
J. M. DRENNAN and J. M. BEARE. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **68**, 345–358, 1954. 9 figs., bibliography.

In urticaria pigmentosa there is a congenital abnormality of large areas of the skin, the presence of numbers of mast cells being associated with a tendency to wealing. In this paper from Queen's University and the Royal Victoria Hospital, Belfast, the authors describe 4 cases in which a more intense form of the same lesion was limited to a single small area; they have found reports of 4 similar cases in the literature. In each case there was a pigmented macule of the skin which wealed intensely on rubbing and was packed with mast cells. The oldest patient was 2 years 2 months and the youngest 2 months. In all the cases the lesion was congenital. In 2 cases it was situated on the flexor surface of the forearm, in one in the lumbar region, and in one on the right scapula. The lesion in the youngest patient had a core of primitive cells which were differentiating into mast cells peripherally; in 2 cases the lesion consisted of mature cells; and in one it appeared to be regressing. A high concentration of histamine was found in the lesion in 2 cases and a high concentration of heparin in one.

Study of these cases is believed to have been of value in showing that mast cells are derived from primitive reticulum cells, are phagocytic only when immature, secrete both histamine and heparin, and contain a lipoprotein of importance in the process of secretion. These cases also showed that histamine may be responsible for attracting eosinophils to the lesions, and heparin for the formation of Charcot–Leyden crystals from them. *Bernard Lennox*

1147. **Concentration of Cells from Body Fluids for Cytologic Study**
E. A. MCGREW. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **24**, 1025–1029, Sept., 1954. 7 figs., 2 refs.

A modification of the method of Fawcett and Vallee (*Bull. New Engl. med. Cent.*, 1950, **12**, 224) for the concentration of malignant cells in bloody or turbid effusions has been found to be of value at the University of Illinois College of Medicine, Chicago. Essentially it consists in resuspending the centrifuge deposit in saline, layering the suspension over 21% commercial bovine albumin solution, and recentrifuging. Erythrocytes and much of the other interfering material sink through the albumin solution, whereas malignant cells remain at the junction of the layers and are looked for in smears of material obtained from that level. The method was used in 30 cases and gave positive results in 11, in one of which tumour cells could not be found by any other method. *Bernard Lennox*

1148. **Demonstration of *Histoplasma* and *Coccidioides* in So-called Tuberculomas of Lung. Preliminary Report on Thirty-five Cases**
L. E. ZIMMERMAN. *Archives of Internal Medicine* [*Arch. intern. Med.*] **94**, 690–699, Nov., 1954. 7 figs., 26 refs.

The author suggests that many "coin lesions" of the lung are termed "tuberculoma" in error. In support of this view he describes a study carried out at the U.S. Armed Forces Institute of Pathology, Washington, D.C., on 35 surgically resected discrete pulmonary granulomata from cases in which the pathologist had made a diagnosis of tuberculosis or probable tuberculosis on a histological basis. Sections of all the lesions were stained for acid-fast bacilli by the Ziehl–Neelsen method, and for the demonstration of fungi the periodic-acid–Schiff reaction and the Gridley technique were used. Acid-fast bacilli were found in 6 cases, *Histoplasma* in 19, and *Coccidioides* in 3; in the remaining 7 cases no organisms were demonstrated. It is recommended that the most fruitful site to search for these organisms is the central necrotic area of the lesion.

The author believes that this series, based on cases contributed from many different parts of the country and occurring in Service personnel who had travelled widely, constitutes a representative sample of the over-all incidence of the various types of this lesion in the United States. It is urged that the term "tuberculoma" be reserved for those lesions in which tubercle bacilli have actually been demonstrated. *R. B. Lucas*

1149. **Malignant Synoviomata.** (Злокачественные синовиомы)
V. V. ALYAKRITSKIĬ. *Архив Патологии* [*Arkh. Patol.*] **16**, 71–75, Oct.–Dec., 1954. 3 figs., 11 refs.

The author cites from the Russian literature 13 cases of malignant synovial tumours, only two of which, however, were adequately described from the histological point of view; both of these would seem to have been cases of malignant synovioma, although both were misdiagnosed, one as carcinoma, the other as fibrosarcoma.

Typical malignant synovioma is described as a sarcomatous cellular tumour with numerous clefts and spaces lined by endothelial cells, sometimes with papillary projections. The lining cells may assume an epithelioid appearance and may occasionally lead to a mistaken diagnosis of carcinoma. The author describes 3 personal cases. In the first the tumour probably originated from the suprapatellar bursa, in the second from the synovial lining of the joints between the vertebral processes in the upper thoracic region, and in the third from the processes of the synovial membrane extending along the muscle tendons of the upper arm. The histological appearances are illustrated in three accompanying photomicrographs. *A. Swan*

1150. **Cancer Cells in Urinary Sediment.** [In English]
C. DEDEN. *Acta radiologica* [*Acta radiol. (Stockh.)*] Suppl. 115, 1–95, 1954. 36 figs., 36 refs.

Bacteriology

1151. **Strain Variations and Cross-relationships in Influenza Virus**

K. E. JENSEN. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **44**, 1167–1173, Sept., 1954. 2 figs., 15 refs.

An outline is given of a detailed analysis, carried out at the University of Michigan School of Public Health, Ann Arbor, of the antigenic composition of 42 strains of influenza virus A representative of epidemics which have occurred since 1933. After treatment with periodate the virus can no longer be eluted from erythrocytes to which it has been adsorbed; the stable preparations so obtained are satisfactory for the absorbtion of sera. Ferrets were infected with 29 strains of this virus, and from the convalescent blood 18 strain-specific sera were obtained for use in antigenic analysis. Quantitative estimation of the antigenic constitution of a particular strain was made by determining the residual amounts of the various antibodies remaining after the strain had been used to absorb a sample of the mixed strain-specific sera, which had been so pooled as to produce equal titres of antibody to the various specific antigens. In this way the antigenic " profile " of the strain could be drawn.

Studies of the epidemic strains showed that antigens which had predominated in older strains were often present in small amounts in strains recently isolated, and the author considers that the probability that completely new major antigens will emerge, or that the old will entirely disappear, is not great. The application of this method of antigenic analysis to vaccination against epidemic influenza is discussed. The large number (18) of different antigenic components may seem discouraging, but it is pointed out that with mineral-oil adjuvant vaccines only small quantities of antigen are needed, so that several strains of virus can be combined in a single inoculum. The strains to be used for vaccine production would therefore be selected on the basis of their antigenic " profiles ", the profiles chosen being those which would produce high antibody levels against the broadest range of antigens. *J. E. M. Whitehead*

1152. **Growth Characteristics of Poliomyelitis Virus in HeLa Cell Culture: Lack of Parallelism in Cellular Injury and Virus Increase**

W. W. ACKERMANN, A. RABSON, and H. KURTZ. *Journal of Experimental Medicine* [*J. exp. Med.*] **100**, 437–450, Nov., 1954. 8 figs. 7 refs.

In this study, carried out at the School of Public Health, University of Michigan, Ann Arbor, the action of the antimetabolite fluorophenylalanine (FPA), on the growth *in vitro* of Type-III poliomyelitis virus (Saukett strain) in HeLa cells was examined. Conditions were such that a single sequence of infection was induced. In untreated cultures the curve of the virus titre plotted against time maintained a constant level for 4 to 5 hours and then rose during the following 6 or 7 hours, after which a maximum level was maintained for a further 12 hours. Pathological changes, including increased basophilia and nuclear pyknosis, in the HeLa cells were noted from about the 7th hour onwards.

The addition of 0·1 mg. of FPA to the culture medium before infection prevented multiplication of the virus, and changes in the cells were absent or much reduced. FPA was also effective in blocking virus increase when added not more than 2 hours after infection of a culture, that is, nearly 7 hours before the time of maximum rate of virus production; but although virus multiplication was blocked under these conditions, progressive pathological changes in cells already affected were not prevented.

The virus-blocking effect of FPA added before infection could be reversed by the addition of phenylalanine to the cultures up to 6 hours later. It was shown that the action of FPA was cytostatic rather than cytocidal, and that it had no other detectable effect on HeLa cells. Its action on the virus *in vitro* was related to the age of the infection; inhibition taking effect only on the early stage of virus development. *M. H. Salaman*

1153. **Susceptibility of *Pseudomonas* to Ten Antibiotics *in vitro*. Some Properties of Recently Isolated Strains**

S. S. WRIGHT, K. G. POTEE, and M. FINLAND. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **24**, 1121–1132, Oct., 1954. 1 fig., 20 refs.

At Boston City Hospital (Harvard Medical School) the cultural and biochemical properties of 110 strains of *Pseudomonas* were studied and each strain was tested *in vitro* for susceptibility to 10 antibiotics. The results of the susceptibility tests were compared with those obtained with 32 strains which had been preserved since they were isolated in 1949; also available for comparison were the results of sensitivity tests carried out in 1949 against the antibiotics then available. Polymyxin B proved to be the most active antibiotic, almost all strains being inhibited by 6·3 μg. per ml. Oxytetracycline came next, some strains being sufficiently sensitive to it and to streptomycin—less often to tetracycline—as to suggest possible therapeutic benefit from the use of these antibiotics. All the strains were resistant to 400 μg. of bacitracin and penicillin per ml.

The recently isolated strains, when compared with those isolated in 1949, included a significantly higher proportion resistant to chlortetracycline, streptomycin, tetracycline, and neomycin. The presence of resistant strains appeared to be unrelated to previous antibiotic therapy in particular patients, but reflected an increasing resistance of cross-infecting strains in the hospital. Since tetracycline and neomycin had not been used in the hospital, resistance against them was believed to reflect cross-resistance induced by chlortetracycline and strepto-

mycin respectively. A few strains which were atypical in their cultural properties and defective in pigment production showed a greater susceptibility to antibiotics.

D. G. ff. Edward

1154. **Electron-microscopical Examination of Reiter's Spirochaetes and Nichols's Treponemes.** (Elektronenmikroskopische Untersuchungen an Reiter-Spirochaetales und Nichols-Treponemen)

W. SCHMEROLD and B. DEUBNER. *Hautarzt* [*Hautarzt*] 5, 511–513, Nov., 1954. 9 figs., 10 refs.

The authors have examined specimens of the Nichols strain of treponeme and of the Reiter spirochaete under the electron microscope at the University of Munich, and here describe their findings, several beautifully clear electron micrographs being reproduced in the text. They draw attention to the fibrils, which are clearly seen in most of the pictures, attached to one or other end of the body of the organism, and which in certain specimens are arranged in bundles running the whole length of the body. They support the conclusion reached by Bradfield and Cater (*Nature, Lond.*, 1952, **169**, 944; *Abstracts of World Medicine*, 1952, **12**, 394) that the fibrils are contractile and are probably responsible for the spiral form of the spirochaetes, and suggest that the flagellum-like fibrils described above had been partially detached from the bundles by the destructive effect of the various means of preparation used. The various possible ways in which the fibril bundles may play a part in the movements of the organisms are discussed, with illustrative sketches. [The electron micrographs reproduced are outstanding in their clarity and definition.]

R. D. Catterall

1155. **Effects of Growth *in vitro* with Selected Microbial Associates and of Encystation and Excystation, on the Virulence of *Endamoeba histolytica* for Guinea Pigs**

B. P. PHILLIPS and I. L. BARTGIS. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] 3, 621–627, July, 1954. 1 fig., 11 refs.

The dependence of *Entamoeba histolytica* upon the presence of certain associated bacteria in culture media and in the intestinal tract of animals used for experimental purposes introduces complicating factors which have hindered the study of the pathogenesis of amoebiasis. The discovery that bacteria-free cultures of the amoeba could be obtained by growing it in association with *Trypanosoma cruzi* at first seemed to have removed one of these obstacles, but it was found that in such cultures *E. histolytica* loses its virulence and is incapable of producing amoebiasis in animals. In the work reported here from the National Microbiological Institute, Bethesda, Maryland, which was devoted to the elucidation of the factors governing the virulence of the amoeba, bacteria-free cultures of the amoeba with *T. cruzi* were injected intracaecally at various intervals following the removal (by antibiotics or micro-isolation) of the concomitant flora into guinea-pigs fed on a sterile diet.

It was again shown that a strain of *E. histolytica* which is highly virulent when accompanied by the original flora loses its virulence after prolonged culture (21 to 49 weeks) with the trypanosome alone, though many of the infected guinea-pigs harboured the amoebae in their intestine. However, when injected within 1 to 3 weeks of their isolation from bacteria, such cultures produced acute amoebiasis with typical ulceration, the virulence of these same cultures being definitely less after 5 weeks and decreasing progressively until—at the end of the 8th week—they also became non-invasive. The virulence of the amoebae could be restored by transferring them, together with the trypanosome, to cultures containing only two bacterial species (a streptobacillus *Clostridium perfringens*) or a mixed flora. On re-isolation after 20 days and culture for 1 week with trypanosomes, the amoebae again produced acute symptoms in guinea-pigs, but after the 7th week they once more lost their virulence. Similar results were obtained with bacteria-free cultures derived from amoebic cysts produced during the reactivation process.

It is concluded from these experiments that the accompanying bacteria do not themselves take part in the production of the symptoms of amoebiasis, but that they exert a considerable influence on the virulence of *E. histolytica*. Furthermore it is suggested that periodic encystation—which occurs only in cultures with bacteria, and not in cultures with *T. cruzi*—may possibly be essential for maintaining the virulence of *E. histolytica in vitro*.

C. A. Hoare

1156. **Carbomycin, a Growth-maintaining Factor for *Endameba histolytica* Cultures**

H. SENECA and E. BERGENDAHL. *Science* [*Science*] **120**, 988–989, Dec. 10, 1954. 12 refs.

1157. **A Micromethod for the Serological Diagnosis of Poliomyelitis by Complement Fixation (100 Cases).** (Microméthode pour le diagnostic sérologique de la poliomyélite par la fixation du complément (100 cas))

J. WIRTH. *Praxis* [*Praxis*] **43**, 978–979, Nov. 18, 1954. 12 refs.

The author, writing from the Institute of Hygiene, Geneva, states that a positive result in a complement-fixation test on a patient's serum (in a dilution of 1 in 4) affords valuable evidence of recent infection with poliomyelitis virus. He claims that by the use of a poliomyelitis-virus antigen obtained by concentrating 100-fold the liquid from 40 human-embryo tissue cultures infected with the Mahoney strain (Type 1) of the virus and heating it to 60° C. for 30 minutes a satisfactory micro-complement-fixation test [not described] may be carried out on a single drop of blood obtained from the finger. A total of 107 samples of serum have so far been examined; of 17 from recent cases of poliomyelitis, 8 gave positive complement fixation at a dilution of 1 in 4 [the only dilution tried]; of 7 cases infected more than a year before one was positive, and of 33 suspected cases 3 were positive. Samples from 15 contacts and from 29 control subjects were all negative; one sample out of 6 from laboratory personnel was positive. The method is said to be rapid and reliable.

[As no technical details are given, it is impossible to assess the method used. If it is reliable, it could easily be extended to virus of Types 2 and 3.] *C. L. Oakley*

Pharmacology

1158. **The Nature of the Reflex Vasodilatation Induced by Epinephrine**

C. C. Gruhzit, W. A. Freyburger, and G. K. Moe. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **112**, 138–150, Oct., 1954. 6 figs., 20 refs.

In an attempt to elucidate the mechanism of the reflex dilatation of the blood vessels of skeletal muscle which accompanies the vasoconstriction in other organs resulting from the intravenous injection of adrenaline, experiments were conducted at the State Universities of New York and Michigan on dogs anaesthetized with thiopentone and sodium barbitone. Arterial pressure was recorded with a mercury manometer, and femoral arterial blood flow with a recording differential manometer.

It was first confirmed that the increased blood flow through the vessels of skeletal muscle produced by intravenous adrenaline was due, in part at least, to reflex intervention. Administration of adrenaline to a dog, one of whose limbs was perfused from another dog but still retained its nervous supply (sciatic and femoral nerves), resulted in an increased blood flow in that limb, whereas the administration of an equivalent dose of adrenaline to the donor animal caused active vasoconstriction in the perfused limb. The vasodilatation occurred with doses of adrenaline which failed to cause a rise of arterial pressure, and also when bilateral vagotomy and denervation of the carotid sinus had been carried out, so that the carotid-sinus and aortic-arch reflexes did not appear to be concerned.

When injected into the atria, the pulmonary artery, or the ventricles, adrenaline produced femoral dilatation equal in magnitude to that produced by intravenous injection, whereas little or no dilatation resulted from injection into the cephalic circulation, brachial artery, or aortic arch distal to the brachiocephalic artery; thus the reflex was localized to the cardiac or pulmonary circulation. To eliminate the possibility of stimulating the Bezold reflex the anterior descending branch of the left coronary artery was cannulated and connected to the left common carotid artery and the effects of intracoronary injections of adrenaline and of veratridine compared. Adrenaline produced femoral dilatation equal in degree to that caused by similar doses given intravenously, whereas the effect of veratridine was greater than on intravenous injection. Moreover, vagal blockage (by section or application of ice) completely abolished the dilator response to intracoronary veratridine, but did not prevent the reaction to adrenaline. Other receptors in the lesser circulation likewise did not appear to participate in the reflex.

Further experiments to define the nervous pathway of the afferent limb of the reflex indicated that it must enter the thoracic cord through somatic components of the spinal nerves. With the aid of cross-circulation experiments, the sensory elements were found to be located in the wall of the thoracic aorta and its branches. They appeared to be mechano-receptors.

[This important paper shows that the major part of the dilatation in skeletal muscle produced by adrenaline is accomplished by a reflex, the effect of which is to redistribute the cardiac output. The central connexions and the efferent pathway have not as yet been studied.]

G. B. West

1159. **Marcumar [3-(1′-phenylpropyl)-4-hydroxycoumarin]. A New Anticoagulant**

R. Bourgain, M. Todd, L. Herzig, and I. S. Wright. *Circulation* [*Circulation (N.Y.)*] **10**, 680–684, Nov., 1954. 5 figs., 9 refs.

The effectiveness of a new anticoagulant, "marcumar" (3-(1′-phenylpropyl)-4-hydroxycoumarin), was studied at Cornell University Medical School in animals and human subjects. In starved rabbits anticoagulant activity was detected within 12 hours and continued for 4 to 5 days following the administration of a single oral dose of 2·5 mg. per kg. body weight. After 12 hours the proconvertin time was prolonged to an average of 47 seconds, but the degree of hypoconvertinaemia was not sufficient to increase significantly the dilute or undilute prothrombin-complex times. These latter values were, however, prolonged after 18 hours and reached a maximum value on the 2nd day after the administration of the drug. The administration of higher doses (4 mg. and 10 mg.) gave a response similar to that produced by 2·5 mg. per kg. body weight. The drug was also given to a few rabbits intravenously.

In the study on human subjects, after the control values for the undilute and dilute prothrombin-complex times, the proconvertin time, and the prothrombin time had been determined on the normal human plasma of 40 healthy individuals, a single oral dose of 18 mg. of marcumar was given to 9 patients. Evidence of anticoagulant activity was manifest after 24 hours, and the maximum values for the undilute and dilute prothrombin-complex times occurred on the 3rd day; a normal dilute prothrombin time was observed on the 5th day. When a single oral dose of 21 mg. of the anticoagulant was given to 7 patients it was found to give a similar range of values, except that the activity lasted longer. Marcumar was then administered to several patients suffering from thrombo-embolic disease in an initial dosage of 21 mg. on the first day and 9 mg. on the second, treatment thereafter being continued with 3 mg. daily to keep the dilute and undilute prothrombin-complex times within the therapeutic range. The dosage requirements were found to vary from patient to patient, and in the same patient from day to day. There was also a tendency for the effect to accumulate over a period of time on the same dosage.

The authors conclude that marcumar is a suitable and effective anticoagulant, but that, as with all coumarin derivatives, careful observation and frequent checking of the dilute and undilute prothrombin-complex times are essential. *Robert Hodgkinson*

1160. **Clinical Experience with Dipaxin and with the Combined Use of Prothrombopenic Agents**
R. KATZ, H. DUCCI, W. ROESCHAMANN, and L. TORIELLO. *Circulation* [*Circulation (N.Y.)*] **10**, 685–690, Nov., 1954. 6 figs., 13 refs.

"Dipaxin" (2-diphenylacetyl-1 : 3-indanedione) has been reported as having the most marked prothrombopenic action of a group of compounds which includes dicoumarol, "tromexan", and 17 analogues of the indanedione group. In a study of this substance carried out at Salvador Hospital (University of Chile Medical School), Santiago, the authors found that 24 hours after a dose of 30 mg. of dipaxin was administered orally to 10 patients, 5 showed a prothrombin-complex concentration below 30%. At the 41st hour after administration all had a prothrombin-complex level of between 8 and 28% and this lasted for about 100 hours. By comparison, in none of 10 patients had this level fallen below 30% at the 24th hour following treatment with 300 mg. of phenylindanedione, while of 5 patients given 1,500 mg. of tromexan (ethylbiscoumacetate) all showed a level below 34% at the 24th hour. In 2 patients, in whom the prothrombin-complex level had been reduced below 25% by dipaxin therapy, the administration of 50 mg. of vitamin K_1 intravenously caused a rise of the level to 45% by the 4th hour, and pretreatment values were reached in 24 hours. Such high intravenous doses of vitamin K_1 unfortunately produce a refractory period during which the patient does not respond to the prothrombopenic agent. It is therefore recommended that patients who develop a dangerously low prothrombin-complex level should be given 3 to 5 mg. of vitamin K_1 by mouth, since this dose is sufficient to raise the value to a safe level without making the patient refractory to further anticoagulant therapy.

Dipaxin was used in the treatment of 60 patients suffering from thrombo-embolic disease, an initial dose of 30 mg. being followed by a maintenance dose of 3 to 5 mg. a day. Prothrombin-complex concentrations fell to a level of 30% or less on the 2nd day in all cases, and only 14% of the patients under prolonged treatment presented, in some of the determinations, prothrombin-complex concentrations above 35% (compared with 16% of cases with phenylindanedione, 30% with dicoumarol, and 53% with tromexan). Transient haematuria (in 1·7% of cases) was the only haemorrhagic episode in this series. In order to take advantage of the earlier prothrombopenic effect of tromexan while at the same time eliminating the disadvantage of the wide variation in the response to this drug, 1,500 mg. of tromexan and 30 mg. of dipaxin were given simultaneously to 10 patients. The prothrombin complex at 24 hours was found to be between 37 and 17% in all cases; dipaxin was then used alone for maintenance treatment. In a further 10 cases 1,500 mg. of tromexan and 200 mg. of phenylindanedione were given simultaneously, but in these the prothrombin-complex level varied between 50 and 17%.

It is concluded that dipaxin is a potent prothrombopenic drug, with an induction period between that of tromexan and phenylindanedione. The therapeutic effects of dipaxin are similar to those of these agents and its action is readily counteracted by administration of vitamin K_1. It may be used with tromexan to produce a therapeutic prothrombin-complex level in 24 hours, and this has the advantage of restricting the necessity for heparin to the first day. *Robert Hodgkinson*

1161. **Antagonistic Effect of Oral Vitamin K_1 on the Action of Ethyl Biscoumacetate and Phenylindanedione**
J. N. M. CHALMERS, M. F. DIXON, and W. POLACK. *British Medical Journal* [*Brit. med. J.*] **2**, 956–959, Oct. 23, 1954. 4 figs., 15 refs.

In a series of experiments at St. George's Hospital Medical School, London, healthy subjects and hospital patients were given a single dose of emulsified vitamin K_1 (2-methyl-3-phytyl-1 : 4-naphthaquinone) by mouth while receiving ethyl biscoumacetate or phenylindanedione in therapeutic doses. In patients receiving ethyl biscoumacetate alone the average time taken for prothrombin activity to return spontaneously to normal on withdrawal of the drug was 44·3 hours; when, however, 100 mg. of vitamin K_1 was given with the last dose of this anticoagulant the average time was 10·3 hours. In similar observations on subjects receiving phenylindanedione it was found that the average time taken for prothrombin activity to return to normal after administration of the drug ceased was 61·6 hours, and that this interval was reduced to 12·6 hours when 100 mg. of vitamin K_1 was given with the last dose of the anticoagulant. *A. Brown*

1162. **The Comparative Diuretic Effectiveness of Mercumatilin and Meralluride with and without Concomitant Administration of Ammonium Chloride**
R. C. BATTERMAN. *American Heart Journal* [*Amer. Heart J.*] **48**, 780–784, Nov., 1954. 6 refs.

"Mercumatilin" ("cumertilin") is a mercurial diuretic which can be given either orally or parentally. At the Veterans Administration Hospital, Bronx, New York, its effects were compared with those of other mercurial diuretics, with and without the preliminary administration of ammonium chloride, in a total of 134 patients. It was found that mercumatilin produced a satisfactory diuresis without the concomitant use of ammonium chloride. *James W. Brown*

1163. **Diuretic Effect and Local Tolerance of a New Type of Mercurial Rectal Suppository: a Preliminary Report**
J. W. DALY. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **228**, 440–447, Oct., 1954. 4 figs., 17 refs.

The diuretic response in oedematous patients to administration of suppositories containing mercaptomerin sodium is described in this paper from the Jefferson Medical College and Hospital, Philadelphia. Each suppository contained 0·5 g. of mercaptomerin (equiva-

lent to 165 mg. of mercury), and preliminary experiments on animals showed that the drug had an effect on the kidney characteristic of that of mercury, and there was no significant irritation of the rectum. One suppository was administered each night or every second night for periods of one week to 6 months to 25 patients with oedema, the treatment being interrupted at intervals for control observations. Diuresis was considered adequate when the patient's weight was approximately constant after initial diuresis or when he continued to lose fluid. By this criterion, satisfactory results were obtained in 20 of the 25 patients. No local or general toxic effects were observed. *Bernard Isaacs*

1164. **The Effect of L-Norepinephrine on Cardiac Output in the Anesthetized Dog during Graded Hemorrhage**
J. P. GILMORE, C. M. SMYTHE, and S. W. HANDFORD. *Journal of Clinical Investigation* [*J. clin. Invest.*] **33**, 884–890, June, 1954. 1 fig., 19 refs.

An investigation of the effect of noradrenaline on haemorrhagic shock was carried out at the U.S. Naval Medical Field Research Laboratory, Camp Lejeune, N. Carolina, on dogs anaesthetized with chloralose and urethane. Brachial and femoral arterial pressures were measured with an electromanometer, and cardiac output by the dye injection method.

After control observations of cardiac output, pulse rate, and central venous and arterial pressure had been made, L-noradrenaline was injected intravenously by means of a constant-infusion pump for 10 minutes in a dosage of 0·47 to 1·02 μg. per kg. body weight per minute, after which the observations were repeated. The expected increase in mean arterial pressure was produced, but changes in cardiac output and total peripheral resistance were variable. After the arterial pressure had returned to its original level, bleeding was begun at the rate of 50 ml. per minute and continued until a mean arterial pressure of 50 mm. Hg was reached. This level was maintained for several minutes. Another set of observations was then made before and during the infusion of noradrenaline, which was given at the same rate and for the same time as during the control period. At this stage—the early first stage of haemorrhage—noradrenaline infusion caused a significant increase in cardiac output and mean arterial pressure. The mean arterial pressure was then held at 50 mm. Hg for 75 minutes and the observations repeated. At this stage too—the late first stage of haemorrhage—noradrenaline produced an increase in the cardiac output and mean arterial pressure. The animals were then again bled at a rate of 50 ml. per minute until a mean arterial pressure of 30 mm. Hg was reached, when the observations were repeated. At this stage—the early second stage of haemorrhage—increases in cardiac output and mean arterial pressure were again recorded. Arterial pressure was maintained at 30 mm. Hg for 75 minutes and repeat observations made (the late second stage of haemorrhage), after which all the blood removed was reinfused and, when the blood pressure had become stabilized, a final set of observations made. Both at this stage (the return period) and the previous one noradrenaline caused no significant change in cardiac output or arterial pressure. Although the mean total peripheral vascular resistance rose during the infusion of noradrenaline at all stages, the rise was not statistically significant.

It is concluded that the increase in cardiac output produced by noradrenaline during the early stages was due to an increased stroke volume, since no tachycardia was observed. This increase probably results from a direct effect of the drug on the myocardium or from an increase of venous return.

[These findings supplement clinical observations of the effect of noradrenaline in surgical shock. In cases of moderate haemorrhagic hypotension significant increases in cardiac output and arterial pressure are noted on administration of the drug. After near-fatal exsanguination or peripheral vascular failure, however, noradrenaline appears to be of little therapeutic value alone. Possibly its combination with whole-blood transfusion should be tried.] *G. B. West*

1165. **The Germicidal Action on Human Skin of Soap Containing Tetramethylthiuram Disulfide**
R. L. BAER and S. A. ROSENTHAL. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **23**, 193–211, Sept., 1954. 3 figs., 14 refs.

The germicidal action of a soap containing 1% tetramethylthiuram disulphide upon the bacteria of the hands of healthy subjects was tested quantitatively at University Hospital, New York, a multiple-basin hand-washing technique being employed. It was found that after the soap had been used for one week there was a substantial reduction in the "transient" and "resident" bacterial population of the skin of the hands, the effect being greater and lasting longer than that of soap containing 2% hexachlorophene. Skin micrococci did not develop increased resistance to tetramethylthiuram disulphide even after the soap had been used daily for a week or two. The soap was well tolerated by 301 of 309 patients with various skin conditions, who used it for 2 or more weeks. Patch tests were carried out on 214 of these patients 4 weeks or more after they had begun to use the soap; only one showed any evidence of allergic sensitization to tetramethylthiuram disulphide. *Joyce Wright*

1166. **A New Surface Anesthetic Agent: "Tronothane"**
L. PEAL and M. KARP. *Anesthesiology* [*Anesthesiology*] **15**, 637–643, Nov., 1954. 1 fig., 2 refs.

Among the considerable number of local analgesics now available, none has yet proved to be ideal. Recently at the Wesley Memorial Hospital (Northwestern University), Chicago, the authors have tested a new surface analgesic, "tronothane" (*para*butoxyphenyl gamma-morpholinopropyl ether hydrochloride), which is unique among clinically useful local analgesics in that it contains a morpholino radicle. Because of this structure it was considered unlikely to produce reactions in patients sensitive to other local analgesics, and this was confirmed when as a result of a challenge patch test performed on 69 volunteer subjects who had previously had tronothane jelly applied to the skin for 23 days, only 4 showed sensitivity, an incidence one-fifth of that observed in a

similar test carried out on the same patients with "cyclomethycaine". Gross sensitization did not occur in several patients who were known to be sensitive to other topical analgesic agents.

Toxicity studies on animals showed that tronothane compared favourably with other local analgesics. The acute symptoms of toxicity in mice consisted in stimulation combined with depression, and the typical convulsions produced by other similar drugs did not occur so regularly. The LD_{50} for mice was 460 mg. per kg. body weight and death appeared to be due to respiratory paralysis. When injected into tissues tronothane was found to be relatively irritating as compared with other local analgesics. Solutions of 0·25% to 2% tronothane were instilled into the conjunctival sac of 12 guinea-pigs and the onset and duration of anaesthesia was determined by a multiple-stimulation technique employing a soft wire loop; anaesthesia developed within 1½ to 3 minutes and lasted for 12 to 43 minutes.

In the main clinical trial 858 patients from five departments of the Memorial Hospital received 1% tronothane in various forms. Sensitivity was not encountered in any of these cases, but 32 patients noted a transient, mild, burning sensation which disappeared as soon as analgesia was established. Of 325 obstetric patients with episiotomy wounds and lacerations treated by application of a heavy 1% jelly, 79·4% obtained good or excellent relief from burning and pain. From the Proctology Department "good" or "excellent" results were reported in 92% of 100 patients who had undergone haemorrhoidectomy or repair of anal fissure or who suffered from anal ulcers. A 1% light jelly was used in 192 genito-urinary cases before cystoscopy, "excellent" or "good" results being obtained in 95%. Of 42 dental patients, all children, requiring injections into the gum or with painful tooth cavities treated with tronothane, only 6 (14%) complained of slight pain or discomfort. The anaesthetists reported excellent or good results in 93% of 199 patients in whom endotracheal or Levin tubes smeared with 1% tronothane cream were inserted during anaesthetization. Tronothane cream was also found effective in the relief of sunburn, mosquito bites, and other minor irritations. The authors conclude that "tronothane is an excellent anesthetic agent with minimal sensitivity". *Robert Hodgkinson*

1167. **The Analgesic Effectiveness of Codeine and Meperidine (Demerol)**
L. LASAGNA and H. K. BEECHER. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **112**, 306–311, Nov., 1954. 1 fig., 11 refs.

The comparative analgesic potency of codeine and of pethidine ("meperidine") was studied at Massachusetts General Hospital (Harvard Medical School), Boston, in patients suffering severe, constant pain after various operations. Each patient was given injections of morphine phosphate alternating with either codeine phosphate or pethidine hydrochloride. The injections were given subcutaneously, the dosages of the three drugs per 70 kg. body weight being: morphine, 10 mg.; codeine, 30 to 120 mg.; and pethidine, 25 to 100 mg. The degree of analgesia was assessed from the patients' observations by technicians who were unaware of the particular drug given; the duration of pain relief was taken as the period which elapsed before another injection was requested.

The analgesic potency of codeine increased as the dose was raised from 30 to 120 mg. per 70 kg. body weight, pain relief increasing from 43·7 to 65·8% while the duration of pain relief increased from 4·87 hours with 60 mg. to 7·12 hours with 120 mg. The principal advantage with doses of more than 60 mg. was a prolongation of the effect. It is pointed out that the analgesic effect of codeine even in doses of 120 mg. was no greater or more prolonged than that of 10 mg. of morphine. There was rapid relief of pain after administration of 50 or 100 mg. of pethidine which was comparable in degree and duration to that obtained with 10 mg. of morphine.

The incidence of side-effects after administration of 60 to 120 mg. of codeine, or 10 mg. of morphine, or saline was studied in 10 healthy subjects, the drugs and the placebo being given in random order at 3-day intervals. It was found that the incidence of side-effects and the depression of the respiratory minute volume response to inhalation of 5% carbon dioxide in oxygen were of the same order of magnitude after administration of codeine as after morphine, and that injection of saline produced few side-effects and no significant depression of respiratory response.

The authors suggest that most clinicians underrate the potency and the toxicity of codeine given parenterally. Although 50 or 100 mg. pethidine can be substituted for a standard dose of morphine in many clinical conditions, its effect "appears neither much better nor much worse" than that of morphine. *Thomas B. Begg*

1168. **The Analgesic Effectiveness of Nalorphine and Nalorphine–Morphine Combinations in Man**
L. LASAGNA and H. K. BEECHER. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **112**, 356–363, Nov., 1954. 1 fig., 19 refs.

In this paper the authors describe a study of the analgesic efficacy and the side-effects of "nalorphine" and a combination of nalorphine and morphine.

It was found that a dose of 5 mg. of nalorphine produced unpleasant reactions comparable with those observed after administration of 10 mg. of morphine, but had no significant analgesic effect, whereas a dose of 10 mg. or one of 15 mg. had a significant analgesic effect. The simultaneous injection of 2 mg. of nalorphine and 10 mg. of morphine did not influence the ability of morphine to induce analgesia or respiratory depression and subjective side-effects; further, injection of 5 mg. of nalorphine simultaneously with 15 mg. of morphine did not reduce the side-effects of the morphine alone. The only evidence [albeit slender] that nalorphine alleviated the disadvantages of morphine was found in the fact that whereas 15 mg. of morphine caused more side-reactions than 5 mg. of nalorphine, 15 mg. of morphine with 5 mg. of nalorphine caused reactions equal to those after 5 mg. of nalorphine.

A subcutaneous injection of 10 mg. of nalorphine was given to 6 healthy subjects, who were asked to describe their impressions during the next 6 to 8 hours. All complained of drowsiness, lack of concentration, slowing of the mind, blurring of vision, nausea, and various bizarre sensations; one patient experienced a sense of exhilaration.

[The demonstration of an analgesic action of nalorphine in man is in contrast to several reports on the findings in animals, but the reactions with effective doses will preclude the use of this drug as a practical analgesic. It appears difficult to find " ideal " mixtures of morphine and nalorphine which will produce analgesia without troublesome side-effects. Although the experiments described in this paper show that nalorphine does not antagonize mild respiratory depression due to morphine, it is well recognized clinically that it alleviates severe morphine depression.] *Thomas B. Begg*

1169. **Barbiturate Studies. II. Correlation between Clinical Condition and Blood Barbiturate Levels**
I. SUNSHINE and E. R. HACKETT. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **24**, 1133–1138, Oct., 1954. 3 figs., 9 refs.

The correlation between the blood barbiturate level and the clinical condition of 27 patients suffering from barbiturate poisoning was studied at the Western Reserve University, Cleveland, Ohio. Blood samples were taken when the patient was admitted to hospital, 12 hours later, and at 24-hour intervals thereafter, and were analysed by Goldbaum's technique, which determines the amount and type of barbiturate present. In some cases 24-hour samples of urine were also collected and analysed to determine renal excretion. The blood barbiturate level was estimated in each of five arbitrary stages in the clinical progression of barbiturate intoxication.

Study of these cases showed that patients who were comatose but whose reflexes were present recovered without special treatment. An initial blood barbiturate level of more than 4 mg. per 100 ml. indicated serious illness except in the case of phenobarbitone poisoning, when an initial blood level higher than 6 mg. per 100 ml. was serious. There was a good correlation between the clinical condition and the blood barbiturate level, any departure from this suggesting some additional causative factor, such as trauma or synergistic action with other drugs. The blood phenobarbitone level was found to have a half-life of 3 days. Studies of renal clearance in several cases indicated considerable tubular reabsorption of barbiturates. *Norval Taylor*

1170. **Modification of Traumatic Shock by Adrenergic Blocking Agents**
E. Z. LEVY, W. C. NORTH, and J. A. WELLS. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **112**, 151–157, Oct., 1954. 13 refs.

In experiments carried out at Northwestern University Medical School, Chicago, rats were subjected to traumatic shock by placing them for 15 minutes in a rotating drum in which were projecting shelves. Most normal animals survived this procedure but died during the next 24 hours, a relationship existing between the number of turns of the drum and the mortality. The protective action of certain adrenergic blocking agents was then tested by injecting them intraperitoneally 1 to 30 minutes before tumbling was started and observing the effect on mortality. Administration of " dibenzyline " (0·25 mg. per kg. body weight), dihydroergotamine (0·5 mg. per kg.), phentolamine (2 mg. per kg.), " SY-28 " (0·25 mg. per kg.), piperoxan (0·5 mg. per kg.), and tolazoline (2 mg. per kg.) resulted in each case in a significant reduction in the total mortality.

The authors found, however, that these drugs also appeared to cause a significant increase in the mortality during the period of trauma, which suggests that sympathetic discharge has a protective effect during trauma, although ultimately detrimental to survival at a later stage. *G. B. West*

1171. **Investigation of the Effects of Prolonged Pharmacological Sleep in Animals.** (Опыт исследования длительного медикаментозного сна у животных.) (Предварительное сообщение.)
B. S. BAMDAS, D. I. LANDO, A. P. LEVKOVICH, Y. B. NULLER, G. K. TARASOV, and V. S. TSIVIL'KO. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. i Psikhiat.*] **54**, 773–787, Sept., 1954. 12 figs., 8 refs.

Although sleep therapy has been used extensively in the U.S.S.R. in the treatment of many conditions, no comprehensive study of its systemic and neurological effects has so far been undertaken. The authors have now initiated such a study at the Postgraduate Medical School and Institute of Psychiatry, Moscow, and here report preliminary results of their observations on 2 dogs subjected for 10 days to sleep induced by barbiturates and " adalin " (carbromal). They discuss the effectiveness of various drugs, alone and in combination, in maintaining established conditioned reflexes and their effect on the respiration, electrocardiographic findings, blood picture, and blood chemistry.

The dogs were killed 6 days after termination of the period of induced sleep and the brain examined histologically. During administration of the drugs the clinical and physiological findings had indicated a varying extent of toxic change analogous to that observed in human subjects during sleep therapy, while post mortem the morphological changes in the central nervous system, such as cellular swelling, hydropic changes, and some degree of nuclear degeneration and cytolysis, were suggestive of early toxic encephalopathy. While admitting that conclusions based on this small series can be of only limited value in the evaluation of sleep therapy the authors urge the need for further work in the search for safer drugs for the induction of prolonged sleep. *L. Crome*

1172. **Comparative Potency of Newer Anticholinergic Drugs in Man as Determined by Sigmoid Motility Technique**
M. H. SLEISENGER, M. EISENBUD, and T. P. ALMY. *Gastroenterology* [*Gastroenterology*] **27**, 829–837, Dec., 1954. 2 figs., 9 refs.

Chemotherapy

1173. **The Absorption, Toxicity and Experimental Antituberculous Action of 5-Amino-7-Methyl-1 : 2 : 4 : 6-Tetra-azaindene**

J. FRANCIS, A. R. MARTIN, F. L. ROSE, and A. SPINKS. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **9**, 437–440, Dec., 1954. 5 refs.

5-Amino-7-methyl-1 : 2 : 4 : 6-tetra-azaindene (7438) was well absorbed when given orally to mice, guinea-pigs, dogs and monkeys; it was fairly persistent in the blood and passed freely into the cerebrospinal fluid of dogs. Mice tolerated repeated oral doses of 250 mg. per kg., but guinea-pigs, dogs, and monkeys tolerated repeated doses of only 25 to 50 mg. per kg. Doses of 100 mg. per kg. in dogs produced necrosis of the liver and death.

At its maximum tolerated doses, 7438 was of the same order of effectiveness as *p*-ethylsulphonylbenzaldehyde thiosemicarbazone against established tuberculosis in mice. The drug was considerably less effective than streptomycin against established tuberculosis in mice and guinea-pigs. Against cerebral tuberculosis in guinea-pigs 7438 had no effect, whereas streptomycin given systemically caused a 50% increase in the mean survival time. It is concluded that 7438 is unlikely to be useful in the treatment of human tuberculosis.—[Authors' summary.]

1174. **The Effect of Cyanacetic Acid Hydrazide on Tubercle Bacilli *in vitro*.** (Cyanacethydrazids verkan pa tuberkelbaciller *in vitro*)

N. OKER-BLOM and N. RISKA. *Nordisk Medicin* [*Nord. Med.*] **52**, 1302–1304, Sept. 16, 1954. 3 refs.

In tests of sensitivity to cyanacetic acid hydrazide (" cyanazid ", " reazid ") the growth of all of 30 strains of *Mycobacterium tuberculosis* isolated from patients with pulmonary tuberculosis was shown to be inhibited by a concentration of 1 mg. per ml. of Youmans's or Dubos's medium, that of 11 by 0·1 mg. per ml., and of 1 by 0·01 mg. per ml. after 28 days' incubation. Inhibition occurred at lower concentrations when the tubes were incubated for 21 days or less, the difference presumably being accounted for by loss of the drug during incubation.

Three strains which were resistant to 0·1 mg. of cyanetic acid hydrazide per ml. were also resistant to isoniazid, but there was otherwise no evidence of cross-resistance to the two compounds. *D. J. Bauer*

1175. **Clinical Observations of Some Malignant Tumors Treated with Sarkomycin, a New Anti-tumor Antibiotic**

S. ISHIYAMA. *Journal of Antibiotics* [*J. Antibiot.*] **7**, 82–87, May, 1954 (received Nov., 1954). 13 figs., 8 refs.

The effect of sarkomycin, an antibiotic derived from *Streptomyces erythrochromogenes*, on malignant tumours was tested at Kanto Teishin Hospital, Tokyo, in 78 inoperable cases. Clinical improvement is reported to have occurred in 26 cases, and in some there was improvement in the histological and radiological pictures. Side-effects of the treatment were negligible. *G. Calcutt*

1176. **Pharmacology and Therapeutic Efficacy of Tetracycline**

M. B. MILBERG, B. KAMHI, and M. M. BANOWITCH. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **4**, 1086–1099, Oct., 1954. 1 fig., 13 refs.

The authors have studied at the Maimonides Hospital of Brooklyn, New York, the absorption, diffusion, serum concentration, urinary excretion, and toxicity of tetracycline when administered orally, in gelatin capsules or coated tablets each containing 250 mg. of tetracycline hydrochloride or in gelatin capsules containing 250 mg. of the trihydrate, to 118 patients with various infections, chiefly of the urogenital and respiratory tracts.

Absorption was observed in 41 unselected patients who were divided into four groups receiving respectively 0·25 g. (10 patients), 0·5 g. (20), 0·75 g. (6), and 1 g. (5) of tetracycline by mouth every 6 hours for periods up to 12 days. At 24 hours the serum concentration ranged from 1·25 to 5 μg. per ml. for the smallest dose to 11 μg. per ml. for the largest dose. The highest concentrations were noted on the 4th day, when the mean figures for the four different dosage levels were 4·25, 7·76, 12, and 16 μg. per ml. respectively. A significant serum level was maintained for 48 hours after medication was discontinued.

Concentration in pleural fluid reached a level comparable with that in the serum, in ascitic fluid it was above 50% of the serum level, and in the cerebrospinal fluid about 25% of serum level. Excretion was rapid and the urinary concentration higher than that observed with tetracycline analogues. With doses of 0·25 g. the urinary concentration was 5 to 1,000 μg. per ml., with 0·5 g. it was 3 to 2,000 μg. per ml., with 0·75 g. it was 125 to 2,000 μg. per ml., and after doses of 1 g. it ranged from 25 to 4,000 μg. per ml. In some cases low urinary levels were associated with poor renal function.

No toxic effects were noted in patients receiving 0·25 g. 6-hourly, but one of 20 patients receiving 0·5 g. suffered from diarrhoea. With higher doses the incidence of side-effects rose, 4 out of 6 patients receiving 0·75 g., and 2 out of 5 receiving 1 g. 6-hourly suffering from nausea. Neither the mode of presentation (tablet or capsule) nor the radical employed (hydrochloride or trihydrate) appeared to influence the incidence of side-effects. The clinical response was similar to that seen in comparable series of patients treated with chlortetracycline and oxytetracycline. *Bernard Freedman*

1177. **An Antagonist of Streptomycin and Dihydrostreptomycin produced by *Pseudomonas aeruginosa***

J. W. LIGHTBOWN. *Journal of General Microbiology* [*J. gen. Microbiol.*] **11**, 477–492, Dec., 1954. 6 figs., 22 refs.

Infectious Diseases

1178. **The Treatment of *Ascaris lumbricoides* Infections with Piperazine**
H. W. BROWN. *Journal of Pediatrics* [*J. Pediat.*] **45**, 419–424, Oct., 1954. 14 refs.

Although there are numerous reports of success with piperazine in the treatment of infestation with *Ascaris lumbricoides*, there is little general agreement concerning the number of consecutive days on which the drug should be given to achieve a cure. In this paper from the College of Physicians, Columbia University, the author describes the results of administration of this drug by mouth for 2 to 5 consecutive days to 51 infected children. Each child was given 5 ml. twice a day of a syrup containing piperazine citrate (equivalent to 1 g. daily of piperazine hexahydrate). The child received a normal diet without fasting and no purgative was given.

As a result of the treatment all the roundworms were passed by 46 of the patients, many of the worms being reported to be live. The percentage reduction in the egg count for the whole group was 95·2. The author considers that failure of treatment was not related to the dosage of piperazine, but rather to the location of the worms in the host, to the presence of certain foodstuffs, or to different absorption rates. A second course of treatment was given to 4 of the children who did not respond to the first and 3 of them were cured. No side-effects were observed. *Marianna Clark*

VIRUS DISEASES

1179. **Pain Associated with Acute Poliomyelitis. Neurologic and Therapeutic Considerations**
P. BENDZ. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **88**, 141–147, Aug., 1954. 2 figs., 22 refs.

In acute poliomyelitis pain may occur either in the preparalytic stage or after paralysis has developed; it may be in the form of spontaneous aching, both continuous and paroxysmal, or it may be present in the form of tenderness. It is often a troublesome factor and may predispose to contractures. The author of this paper from the Infectious Diseases Hospital, Stockholm, discusses both the pathogenesis of the pain and measures for its relief. From personal observation of some 200 cases of poliomyelitis with paralysis of the limbs he concludes that the pain has both a neuralgic and a myalgic origin, and that its source is to be found in those nerve roots—dorsal and ventral—which arise from the affected segments of the spinal cord, the neuralgic element being referable to the dorsal roots and the myalgic to the ventral roots.

Discussing local and general measures for the relief of pain the author first refers to methods of producing hyperaemia—for example, by hot baths or packs. Friction heat by massage or the reactive hyperaemia which develops after a limb has been deprived of its blood supply for a few moments by means of an inflatable cuff will also alleviate the pain; the latter method has been found to influence painful muscle contractures of the limbs due to "muscle spasm", especially in children. As soon as pain is relieved the arm or leg can be straightened or the foot-drop corrected. Vasodilators such as "benzazoline" (tolazoline) in fairly large doses have been used, but the side-effects are often worse than the pain itself, and the analgesic results are uncertain. Subcutaneous injection of a local analgesic where the pain is maximal is of benefit, particularly in the case of pain in the lumbar region and pain in circumscribed areas. The author has found caffeine, alone or combined with phenacetin, the most effective treatment. *J. V. Armstrong*

1180. **Encephalomyelitis Associated with Poliomyelitis Virus. An Outbreak in a Nurses' Home**
E. D. ACHESON. *Lancet* [*Lancet*] **2**, 1044–1048, Nov. 20, 1954. 23 refs.

The author presents a detailed description of a small epidemic involving 14 nurses resident at the Middlesex Hospital, London, in which there was involvement of the central nervous system and intense myalgia. The outbreak seemed similar in many ways to four others reported since 1950 in various parts of the world, all of which bore some resemblance to poliomyelitis although not being typical of it. In the present instance there was no history of recent cases of poliomyelitis in the hospital or in neighbouring boroughs. In proportion to the nursing population at risk the attack rate was about 2%; infection was probably spread by droplets and the speed and route of spread suggested the presence of a large number of intermediate carriers. The incubation period seemed to be about 17 or 18 days.

The characteristic clinical features of the outbreak were the association of severe muscular pain affecting the back, limbs, abdomen, and chest with evidence of mild involvement of the central nervous system, particularly of the pyramidal tracts, the posterior columns, and the cranial nerves, rather than of the anterior horn cells. Lumbar puncture was performed in 6 cases, in all of which the cerebrospinal fluid was found to be normal; the blood count and result of the Paul–Bunnell test were also normal. Of the 14 patients, 7 recovered without sequelae and were discharged in a month; mild pyramidal signs persisted, however, in 4 of the remaining 7, and excessive fatigue and intermittent backache were present in several cases for 3 or 4 months.

At first the outbreak was thought to be one of poliomyelitis and in one case Type-3 poliomyelitis virus was actually isolated from the stools. However, in no case was there residual flaccid paralysis, and other points, such

as the mildness of the fever, the comparatively slow development of symptoms over a period, and the presence of extensor plantar responses seemed to militate against the diagnosis of poliomyelitis. Bornholm disease was also considered, but tests for infection with Coxsackie viruses were negative, as were also those for mumps, lymphocytic choriomeningitis, and leptospiral infection. The author concludes that if this outbreak was due to poliomyelitis virus then the characteristics of this disease would appear to be changing. Alternatively, assuming that the cause was not poliomyelitis and that the isolation of Type-3 poliomyelitis virus in one case was fortuitous, then the outbreak may have been due to a neurotropic agent or agents epidemiologically linked with poliomyelitis, but less virulent and requiring different methods of isolation. *J. V. Armstrong*

1181. **Myocarditis in Poliomyelitis.** (Zur Frage der Myokarditis bei Poliomyelitis)
H. UFLACKER. *Archiv für Kinderheilkunde* [*Arch. Kinderheilk.*] **149**, 144–155, 1954. 2 figs., 47 refs.

During an epidemic of poliomyelitis in Hessen in 1952 the electrocardiograms (ECG) of 62 young patients aged 1 to 14 were studied for evidence of myocarditis. It was found impossible to predict by clinical methods in which cases an abnormal ECG might be expected, except in 3 in which there was a high fever and tachycardia. Abnormalities in the ECG were noted in 21 cases showing no clinical evidence of myocarditis. These took the following forms: sinus tachycardia, 3 cases; PQ interval prolonged, 3; widening of QRS, 1; depression of the ST segment in two or more leads, 3; prolongation of QT, 7; abnormal T waves, 20; and alteration of electrical axis, 4 cases. In the ECGs taken at regular intervals throughout the course of the disease it was observed that T-wave abnormalities occurred most markedly in the 3rd or 4th week. The most marked ECG changes were seen in patients most severely affected by the disease. In 19 cases there was an increase in blood pressure, but only 11 of these patients showed an abnormal ECG.

In many cases the abnormality in the ECG continued for several months, but except in cases with bulbar paralysis, in which the combination of myocarditis and respiratory difficulty seemed to increase the likelihood of sudden collapse, the prognosis was generally favourable and no special treatment was undertaken. In 2 cases coming to necropsy histological evidence of interstitial myocarditis was found. The author concludes that myocarditis is a complication to be expected in a proportion of cases of poliomyelitis. *G. S. Crockett*

1182. **Artificial Ventilation in Poliomyelitis**
C. M. AARSVOLD. *Journal of the Oslo City Hospitals* [*J. Oslo City Hosp.*] **4**, 153–163, Nov., 1954. 5 refs.

During the 6 years 1946–51, 80 patients with poliomyelitis were treated at Ullevål Hospital, Oslo, in the tank respirator, 65 of whom died during treatment and 5 later from sequelae of poliomyelitis.

The present paper is concerned with the treatment of poliomyelitis since the introduction of artificial ventilation with positive pressure as a result of experience in the Copenhagen epidemic of 1952–3. During the past year 19 patients have been treated with artificial respiration, 5 in tank respirators, 1 with a cuirasse respirator, and 13 with tracheotomy and positive-pressure ventilation, partly manually performed and partly with mechanical respirators of various commercial types. Of these 13 patients, 4 died; in 2 cases death was due to extensive encephalitis, and in 2 to suffocation due to obstruction of the bronchi by tenacious secretion. The mechanical respirators used all proved satisfactory, but the nursing staff had to be extremely watchful to correct leaks in the respiratory system and to prevent accumulation of secretion.

If it was thought the patient was being under-ventilated and the situation was not critical the alkali reserve of the blood was determined, but in emergencies the *p*H of the urine was tested with indicator paper. It was found that when the alkali reserve was maintained between 50 and 60 volumes % and the urinary *p*H between 5·5 and 7·0 the patient felt well. Any fluctuation beyond these limits resulted in increasing discomfort. Measurements of the blood pressure were found of little value. [This is contrary to Danish experience.]

Pulmonary complications such as atelectasis and pneumonia were frequent, atelectasis being due probably to some extent to a too liberal use of oxygen. It was found that it was essential to have an anaesthetist or an otolaryngologist continuously on duty in the wards during the treatment of these cases, while each patient required the exclusive services of 2 attendants. If there was no pharyngeal paralysis, and particularly if the patient was suffering from the spinal type of respiratory failure, the tank or cuirasse type of respirator was preferred, the former being very reliable and requiring less staff for management, although it had the disadvantage that adequate exercise, massage, and nursing attention could not be given without the use of a mask and positive-pressure breathing. Other practical problems of this type of artificial respiration, including the weaning of the patient from the respirator, are discussed.

The author stresses that during the acute stage it is impossible to predict the final result, and that even in the most serious cases where great incapacity might be anticipated satisfactory pulmonary function may be regained. His final conclusion is that the treatment of cases of poliomyelitis with respiratory involvement should be concentrated in centres specially equipped and staffed for the purpose. *J. V. Armstrong*

1183. **Tracheotomy in Poliomyelitis**
H. LINDEMAN. *Journal of the Oslo City Hospitals* [*J. Oslo City Hosp.*] **4**, 164–171, Nov., 1954. 4 figs., 8 refs.

Of 485 cases of poliomyelitis admitted to Ullevål Hospital, Oslo, since 1951, tracheotomy was performed in 35, with 14 deaths. Most of these deaths occurred within 2 or 3 days of the operation (there were no operative deaths) and were due to complications arising out of the tracheotomy in 2 cases, to meningoencephalitic lesions in 4, and to a combination of the two in 8 cases.

Tracheotomy was performed if pooling of saliva in the pharynx was considered likely to cause obstruction to the

airway. The high operation was used, but the opening was made below the first tracheal ring to guard against stenosis and granulation in the subglottic area. Most of the patients so treated received some kind of artificial respiration. This was generally by positive inflation with a manually operated respirator in the critical early stage, the patient being transferred to a mechanical respirator as soon as possible. Four of these patients were still receiving some form of artificial respiration during the greater part of the day 7 months later.

The suggestion is made that the high incidence of pulmonary complications with this form of artificial respiration may be due in part to the use of rubber tubes instead of silver cannulae. To prevent atelectasis frequent suction with tapping of the chest wall should be carried out, and bronchoscopy if necessary. Crust formation with obstruction of the airway may occasionally occur and efforts should be made to prevent drying of the secretions by effective humidification of the inhaled air, by adequate fluid intake, and by the instillation of a 3 to 5% solution of sodium bicarbonate, saline, " tyrosolvin ", and " nebacetin ". Inhalation of sodium laurylsulphonate (0·1%) has also proved useful. The administration of pure oxygen should be avoided because of its drying effect on the bronchial mucosa. Difficulty occurs with the ordinary type of curved endotracheal tube owing to pressure on the tracheal mucous membrane with erosion of the tracheal wall, and a cannula provided with a loose inflatable cuff is preferable, this being inserted as soon as possible after tracheotomy.

The author concludes by stressing the importance of the establishment of specialist teams for the treatment of these cases, based on centres staffed with nurses familiar with the problems involved. *J. V. Armstrong*

1184. **Studies on Some Clinical Features of Poliomyelitis: 1. The Relation of the Clinical Features in Bulbar Poliomyelitis to Tonsillectomy Status. 2. Interrelations between the Clinical Features of Poliomyelitis, with Comments on Vomiting, Portal of Entry and Pathogenesis**

R. V. Southcott. *Medical Journal of Australia* [*Med. J. Aust.*] **2**, 845–852 and 885–891, Nov. 27 and Dec. 4, 1954. 27 refs.

1185. **Acute Retinal Periphlebitis Associated with Infectious Mononucleosis**

B. R. Jones. *Transactions of the Ophthalmological Society of the United Kingdom* [*Trans. ophthal. Soc. U.K.*] **74**, 119–130, 1954. 8 figs., 27 refs.

Infectious mononucleosis is much more variable in its clinical picture than is generally recognized. Almost any tissue of the body may be affected, while the more characteristic features—fever, malaise, cough, and enlargement of lymph nodes and spleen—may be lacking, the diagnosis depending on the typical blood picture, an initial polymorphonuclear leucocytosis being followed by a mononucleosis of 50% or more with a preponderance of characteristic large lymphoid cells. Ocular involvement has been reported in 103 cases observed during an epidemic in New Zealand, and has also been reported elsewhere. The lesions include dacryoadenitis, conjunctivitis, scleritis, choroiditis, retinal phlebitis, macular oedema, and optic neuritis.

A case is described of unilateral retinal periphlebitis which resembled thrombosis of the central retinal vein except for unusual perivascular cuffing. The diagnosis of infectious mononucleosis was based on the clinical features of the initial attack and on the typical blood picture. The nature and implications of the perivascular cuffing are discussed. *A. Lister*

BACTERIAL DISEASES

1186. **Chloramphenicol in Typhoid Fever: a Review of 110 Cases**

K. C. Watson. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **48**, 526–532, Nov., 1954. 23 refs.

Chloramphenicol was given in the treatment of 110 sporadic cases of typhoid fever seen at Grey's Hospital, Pietermaritzburg, between January, 1953, and June, 1954. The ages of the patients (98 Bantu, 8 Indian, and 4 European) ranged from 10 months to 70 years, and the sexes were about equal. In all cases there was bacteriological confirmation of the diagnosis, in most cases by isolation of *Salmonella typhi* from blood clot and whole blood and in a few by isolation of the organism from the faeces.

A leucopenia below 5,000 cells per c.mm. was present in only 44 of the patients. Clinically, the disease was severe in 22, moderately severe in 66, and mild in 22. Although the clinical picture was characteristic in all cases, almost half were admitted with a diagnosis of suspected pneumonia; true bronchopneumonia as a complication was, however, observed in one case only.

None of the patients in this series received a loading dose of chloramphenicol. As a general rule severely ill patients were given 3 g. daily for 2 to 3 days, followed by 2 g. daily until they were afebrile, and then 1 g. daily for 10 to 12 days after defervescence. In moderate and mild cases the doses were smaller.

Response to treatment was usually good, temperature falling in about 4 days and signs of toxaemia disappearing rapidly. Blood culture was negative within a short time, but the effect of the treatment on antibody formation was variable, rising titres being observed in a number of cases although the antibiotic was given in the first few days of the illness. In general, however, the later treatment was started, the higher the titres obtained. The drug did not appear to have any effect on the incidence of haemorrhage (one case) and perforation (2 cases). Other complications were few. There were 6 deaths, including one from perforation and 5 from myocarditis. None of these 6 patients appeared to respond to treatment. The incidence of relapse (7 cases) was related to the duration of treatment rather than to the total dosage employed, being lower when the course was prolonged. Chloramphenicol had no appreciable influence on the carrier state.

The author recommends a high-calorie diet in severe cases, with careful maintenance of water and electrolyte

balance. Vitamin supplements were given to all the patients. Cortisone was tried in 2 cases, with dramatic improvement in one.

Discussing the results the author, while admitting that chloramphenicol has radically altered the outlook in typhoid fever, does not believe that it is the final answer to the problem of treatment. He quotes the work of others who have used T.A.B. vaccine with chloramphenicol to stimulate antibody formation and so decrease the relapse rate. Finally he points out that, contrary to some published findings, toxic reactions were observed in only 11 patients in his series, and none of these was serious.

[The results obtained are very similar to those reported by others, although not all would agree that chloramphenicol has no effect on the incidence of haemorrhage and perforation if given early enough in the disease.]

J. V. Armstrong

1187. **Treatment of Tracheobronchial Diphtheria with Varidase.** [In English]

M. BLECHNER. *Acta medica orientalia* [*Acta med. orient. (Tel-Aviv)*] **13**, 137–140, July–Aug., 1954. 1 fig., 5 refs.

" Varidase " contains the enzymes streptokinase (SK), or fibrinolysin, and streptodornase (SD), or deoxyribonuclease, which are antigens of the haemolytic streptococcus. SK acts indirectly on fibrin or fibrinogen as part of a fibrinolytic system: it activates a fibrinolytic enzyme in human serum (plasminogen) and this sytem splits fibrin into polypeptides. SD on the other hand causes depolymerization of deoxyribonucleoprotein and deoxyribonucleic acid into fragments. These two compounds are the main constituents of cell nuclei, and constitute 50 to 60% of the sediment of purulent exudates. SK and SD acting together thus change purulent exudates into a thin non-viscous fluid. SD acts only on extracellular nucleoprotein and does not attack living cells. SK and SD act at *p*H 6 to 8, their local irritative action producing enough serum to act as a buffer.

Diphtheritic membrane, obtained through a tracheotomy opening, was incubated *in vitro* with varidase at 38° C. for 30 minutes and became disintegrated, sinking to the bottom of the tube. The results of this experiment encouraged the author to try intratracheal administration of varidase in 4 cases of diphtheria at Government Hospital, Sarafand. A few drops of varidase were instilled into the tracheotomy tube of 4 young children with laryngo-tracheal diphtheria who were not breathing well some hours or days after tracheotomy had been performed. This permitted the ready removal by suction of mucomembranous material, with consequent striking relief of respiratory distress. Further trials of this adjuvant to tracheotomy in diphtheria appear to be indicated.

[This would seem to be a useful and possibly also a life-saving measure in certain tracheotomized patients with laryngo-tracheo-bronchial diphtheria. It may be pointed out, however, that membrane in such cases can often be removed piecemeal in successive operations simply by suction through a laryngoscope *per viae naturales*. This procedure obviates tracheotomy and its serious complications,—for example, pneumothorax and tracheo-oesophageal fistula—some of which occurred in the cases described.]

H. Stanley Banks

1188. **Treatment of Tetanus with Curarisation, General Anaesthesia, and Intratracheal Positive-pressure Ventilation**

H. C. A. LASSEN, M. BJØRNEBOE, B. IBSEN, and F. NEUKIRCH. *Lancet* [*Lancet*] **2**, 1040–1044, Nov. 20, 1954. 1 fig., 7 refs.

The authors have applied their method of treatment in cases of bulbar poliomyeltis by tracheotomy and positive-pressure ventilation—which proved so successful at the Blegdam Hospital, Copenhagen, during the poliomyelitis epidemic of 1952—to the treatment of cases of severe tetanus in which complete curarization seemed to be the only means of preventing convulsions and saving the patient's life. In general, routine measures such as tetanus antitoxin, penicillin, excision of the wound (where possible), and sedation were used, but if the patient failed to respond to this, tracheotomy was performed and a cuffed endotracheal tube inserted. Anaesthesia with equal parts of nitrous oxide and oxygen was given intermittently, and if necessary the patient was curarized. This, besides controlling the convulsions, facilitated the application of manually controlled positive-pressure ventilation through a to-and-fro absorber system.

Of 4 patients so treated, 3 made a good recovery; the fourth probably recovered from tetanus, but succumbed to septicaemia, myocarditis, and granulocytopenia. The first of the 4 cases was remarkable for the fact that the patient, a boy of 10 years, was kept continuously under gas and oxygen anaesthesia for 17 days. Curare and pentobarbitone were administered by continuous intravenous drip. Careful observation was kept on the heart, blood pressure, and liver and renal function during the entire period. Nutrition and electrolyte balance were maintained through a stomach tube, and the patient made a complete recovery. The second patient, a boy aged 11, had been doing well under routine treatment until 14 days after admission, when a lightning attack of convulsions set in. The patient was therefore tracheotomized and given intermittent gas and oxygen anaesthesia whenever convulsions threatened. His condition was critical for 14 days, but after that he made a steady recovery. During the critical period frequent bronchial aspiration and bronchoscopy were needed because of crust formation and blocking of the tube with secretions.

The third case, in a boy aged 15, also presented difficulties in regard to keeping the airway free of secretion after tracheotomy. The patient also developed a very high temperature, and had to be given curare as well as gas and oxygen owing to the severity of the attacks. He developed myocarditis and severe leucopenia, and 19 days after admission blood cultures revealed the presence of septicaemia due to *Bacterium coli*, probably originating from a previous infection of the bronchial tree with this organism. The patient succumbed to this infection. The fourth patient, a man of 50, also developed myo-

carditis and granulocytopenia. He was treated along the same lines as the others, but required only short periods of assisted respiration with gas and oxygen. Apart from one short period of anxiety, progress was generally satisfactory and the patient was discharged in good health.

Little has been known previously about the complications of severe protracted tetanus, since the patients seldom survived, but it is probable that the myocarditis and bone-marrow depression which occurred in 2 of these cases were due to the tetanus toxin. However, it is possible that the sedative drugs used, which included pentobarbitone, phenobarbitone, and chloral hydrate, might also be incriminated in the depression of the bone marrow. The authors draw the conclusion [which seems justified] that the toxin of tetanus does not irreparably damage the central nervous system.

[The authors have obviously applied their unique experience of tracheotomy and positive-pressure ventilation to the treatment of severe tetanus with great success. As here used the method seems to offer the best hope of treating those cases which would otherwise prove fatal.]

J. V. Armstrong

SARCOIDOSIS

1189. **Sarcoidosis and the Kveim Reaction**

F. J. ROGERS and J. R. HASERICK. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **23**, 389–406, Nov., 1954. 13 figs., 30 refs.

In 1941 Kveim (*Nord. Med.*, **9**, 169) described a hitherto unrecognized delayed cutaneous reaction in patients with sarcoidosis, consisting in the development, some 2 to 3 weeks after the intracutaneous injection of a suspension of sarcoidal lymph node, of a small indolent papule which resembled sarcoidosis histologically. The reaction was not elicited in patients with tuberculosis or syphilis.

Working at the Cleveland (Ohio) Clinic Foundation the authors of this paper have carried out a histological study of this reaction. Their method of preparing the antigen from surgically removed sarcoidal lymph nodes is described. They found that boiling the antigen decreased its potency and complete elimination of particulate matter by centrifugation rendered it ineffective, but that extraction with ether and removal of the lipids rendered the extract more potent. The presence of hydrocortisone inhibits the development of the papule. The reaction to the test appears to depend on (1) an individual factor, high sensitivity producing more and acuter lesions, and (2) the interval between inoculation and excision of the test site.

The authors had at their disposal for study 12 biopsy specimens of skin positive and 8 of skin negative to the Kveim test, which had been removed between 3 and 42 days after inoculation. Very early positive specimens never show the picture of sarcoidosis, but by 6 to 8 weeks they do; negative specimens show early only a mild perivascular lymphocytic infiltration and return to normal in 6 weeks. The appearance of the positive reaction is described in detail for specimens obtained at 3, 6, 10, 13, 16, 20, 25, and 42 days respectively. After an initial reaction due to the injection, the earliest "specific" change is a perivascular collagen degeneration; in cases of high sensitivity this may exceptionally amount to necrosis. Early immigration of histiocytes by way of the blood vessels is later replaced by the appearance of lymphocytes and epithelioid cells in the areas of degeneration; later still there is giant-cell formation. By the end of 3 weeks the tuberculoid characteristics of the reaction become apparent; after this active proliferative phase the epithelioid tubercles become more "naked", and finally tubercles of sarcoidosis remain at the site of early parenchymal degeneration. It would appear that the presence of lymphocytes represents the active proliferative stage, and the "naked" tubercle of the fully developed Kveim test the end-stage of the granulomatous reaction. The authors conclude by suggesting that the papule of the positive Kveim test is in fact a true sarcoidal lesion and therefore the pathogenesis described above is that of sarcoidosis. The theory that sarcoidosis involves an antigen–antibody mechanism is discussed.

Ferdinand Hillman

1190. **Cortisone Treatment of Sarcoidosis. Experience with Thirty-six Cases**

H. L. ISRAEL, M. SONES, and D. HARRELL. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **156**, 461–466, Oct. 2, 1954. 3 figs., 14 refs.

The results of cortisone therapy in 36 cases of sarcoidosis are described in this paper from the University of Pennsylvania, Philadelphia, the period of observation being 46 months. The patients were selected in so far as all except one had prominent symptoms; 30 of the patients were negroes. The main indications for treatment were respiratory distress, acute uveitis, skin lesions, and acute parotitis. Some improvement was noted in 34 of the 35 patients with symptoms; this was usually more marked in patients with a history of less than 6 months' duration and was most dramatic in 3 patients with swelling of the parotid gland and fever, in whom a response was observed within 24 hours of the administration of cortisone. A rapid improvement was also noted in patients with acute uveitis. Respiratory symptoms responded gradually and less completely. Some of the patients with respiratory distress were unable to tolerate withdrawal of the drug, and 4 died from respiratory insufficiency after 12 to 24 months of cortisone therapy.

Radiological improvement did not parallel the clinical improvement, except for 3 cases in which there was complete resolution of the lung lesions. Parenchymal lung lesions responded more readily than hilar adenopathy. There was a tendency for the miliary type of lesion to respond more readily than the pneumonic type.

Nigel Compston

1191. **A Report of Two Cases of Sarcoidosis with Bronchial Carcinoma**

M. JEFFERSON, W. T. SMITH, A. B. TAYLOR, and K. VALTERIS. *Thorax* [*Thorax*] **9**, 291–298, Dec., 1954. 11 figs., 14 refs.

Tuberculosis

1192. **Studies on the Influence of Exposure to Infection on Tuberculin Reactivity and Morbidity among Neighbours of Tuberculous Subjects.** (Untersuchungen über den Einfluss der Exposition auf die Tuberkulinreaktivität und die Morbidität bei Personen aus der Umgebung von Tuberkulösen)
G. WERNSDORFER. *Schweizerische Zeitschrift für Tuberkulose* [*Schweiz. Z. Tuberk.*] **11**, 455–467, 1954. 4 figs., 6 refs.

The author reports the results of investigations carried out at the Basle Tuberculosis Centre on 1,118 persons (904 adults and 214 children) who were neighbours, workmates, classmates, or members of the family of 231 patients with open pulmonary tuberculosis and 120 with pulmonary tuberculosis without tubercle bacilli in the sputum. Of this total, 572 adults and 139 children had definitely been exposed to infection. All the 1,118 contacts were radiographed, but only 398 of the adults and 201 children were tested with Moro's tuberculin ointment.

Hitherto undetected tuberculosis was found in 18 cases (16 in adults and 2 in children), being primary in 10 and postprimary in 8. Both the children had primary tuberculosis and had been living with an infected adult in whose sputum or gastric juice no tubercle bacilli could be detected. The morbidity from tuberculosis amongst these 1,118 persons was 1·6%, which was higher than that in the population as a whole. This figure is, however, lower than that found in sanatoria, where the degree of infection in the patients and risk of exposure among the staff are greater than in the normal community.

Franz Heimann

1193. **Streptomycin Reactions. Their Characteristic Features, Incidence, Etiology and Means of Prevention**
H. R. C. RICHES. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **48**, 298–307, Oct., 1954. 3 figs., 35 refs.

Because of the relatively high incidence of reactions to streptomycin during long-term therapy, some of which are of a serious nature, an investigation was made at the Brompton Hospital Sanatorium into their aetiology and prevention, 150 adult patients (75 male and 75 female) whose ages ranged from 16 to 56 years being studied. In 55 cases (36%) the patient complained of toxic symptoms on the day of injection, the complaint being of tingling paraesthesiae in and around the mouth in 41 cases, lassitude in 11, vertigo and ataxia in 10, headache in 10, and difficulty of visual accommodation in 7. The symptoms began 1 to 3 hours after the injection of streptomycin and lasted up to 24 hours. In 8 cases they were made worse by exercise and relieved by rest.

In 25 cases the serum and urinary streptomycin levels were determined by the agar diffusion method of Mitchison on two consecutive days, first with the patient at rest after the injection, and then with exercise after the injection. In 21 cases the blood level was found to be higher during activity than at rest, the peak occurring half an hour after injection. In 8 cases the onset of a reaction was shown to occur approximately at the time the maximum blood streptomycin level was reached. Activity after the injection caused no significant change in urinary excretion, the higher blood level being evidently due to an increased rate of absorption. As a result of these findings 10 patients suffering moderate or severe reactions were given their streptomycin at night instead of first thing in the morning, with complete relief of symptoms in 7 cases.

The author emphasizes that liability to reaction varies with the individual, some of his patients with a peak blood streptomycin level of 60 to 90 μg. per ml. having no reaction, whereas one with a peak level of 32 μg. per ml. was almost incapacitated. Finally he makes the important point that any such tendency to develop severe reactions will become a matter of greater importance if the patient is to continue treatment with streptomycin after returning home and starting work.

I. M. Librach

See also Chemotherapy, Abstract 1174.

DIAGNOSIS AND PROPHYLAXIS

1194. **A Fatal Case of Tuberculosis Produced by BCG**
J. MEYER. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **70**, 402–412, Sept., 1954.

A fatal case of tuberculosis due to B.C.G. vaccination is described in this paper from the Finsen Institute, Copenhagen. The patient, a boy aged 7 years, had had measles, German measles, and whooping-cough, but was well at the time B.C.G. vaccination was carried out. Before vaccination he was tuberculin negative, and there was no evidence of contact with a case of tuberculosis before or after vaccination. A fortnight after vaccination the patient felt ill, and one month later an enlarged lymph node was observed in the left axilla. Generalized enlargement of the lymph nodes gradually developed, accompanied by fever, anaemia, and loss of weight. Nine months after vaccination human-type tubercle bacilli were isolated from the gastric contents, but it was thought possible that the examination was not sufficiently exhaustive. In August, 1951, 14 months after vaccination, tubercle bacilli indistinguishable from organisms composing the vaccine were isolated from pus obtained from a lymph node.

All treatment, including chemotherapy, was ineffective. The lesions consisted in multiple enlarged lymph nodes with abscess formation, and ulceration and infiltration

of the skin, chiefly localized to the face, neck, and shoulder region. The urine contained tubercle bacilli. The patient died 2 years and 3 months after vaccination. At necropsy the main findings were generalized enlargement of the lymph nodes, extensive infiltration extending from the lymph nodes, and infiltration of the lungs and kidneys. Histological examination of the lungs revealed diffuse amorphous calcium deposits in the connective-tissue stroma; tubercle bacilli were, however, found only in the single cavity present. Microscopical examination of tissue from the lymph nodes showed widespread caseous necrosis, the tissue being densely filled with tubercle bacilli. *T. M. Pollock*

1195. **An Unusual Cutaneous Reaction in Mental Defectives after Vole Bacillus Vaccination by Multiple Puncture and Its Treatment**

J. A. H. Wylie, D. H. Bennett, and J. Swithinbank. *Thorax* [*Thorax*] **9**, 190–197, Sept., 1954. 8 figs., 18 refs.

In this paper from the Sir William Dunn School of Pathology and Radcliffe Infirmary, Oxford, the authors describe an unusual complication of vole-bacillus vaccination, which has been given to a large number of children, mainly mental defectives, as a means of increasing resistance to tuberculosis. The reaction consists in a non-caseous tuberculous cutaneous lesion closely resembling lupus; a similar reaction has occasionally been observed after vaccination with B.C.G. All cases observed so far have occurred in mentally subnormal children and it is probable that secondary infection plays an appreciable part in the development of these " lupoid " lesions; in some cases, however, they appeared to be associated with intermittent trauma. In a series of over 2,000 vaccinations the incidence of the complication was higher (5·9%) in those under 10 years of age than in those over this age (2·6%). The incidence increased with the density of the vole-bacillus suspension, and was also observed to be higher among mongolian defectives —perhaps due to the quality of their skin. In one group of children of a slightly higher grade of intelligence 6 cases occurred among 44 vaccinated in the thigh, but none occurred among 42 vaccinated in the arm; it is considered that the thigh is more exposed to trauma and secondary infection.

The effects of treatment were studied in two groups containing cases of approximately equal severity. Isoniazid being not then available, the first group (11 patients) were given streptomycin and PAS daily and also old tuberculin intramuscularly every 4th day in increasing dosage until a local or general reaction was noted; tuberculin was then given in a dose just sufficient to maintain a moderate local reaction, consisting in increased vascularity and swelling of the " apple jelly " nodules and erythema of the surrounding skin. The second group (10 patients) were given streptomycin and PAS only; a third group consisting of less severe cases (13) remained untreated and acted as a control. The lesions in the control group did not improve. Those in Group 1 (treated with tuberculin) appeared to heal more quickly than those in Group 2 (receiving streptomycin and PAS only)—an impression which received striking confirmation from histological examination. The advantage conferred by the increased rate of healing, however, was offset by the discomfort produced by the parenteral administration of tuberculin, and it is suggested that the tuberculin might be applied locally as an ointment or jelly.

The authors consider it should be possible to prevent the occurrence of these lesions by guarding against trauma and secondary infection, prompt measures being taken against the latter should it occur, and that the possibility of the complication occurring does not constitute a valid objection to the use of vole-bacillus vaccination. *T. M. Pollock*

TUBERCULOUS MENINGITIS

1196. **The Clinical Course and Treatment of Tuberculous Meningitis in Childhood.** (Klinischer Verlauf und Behandlung der Meningitis tuberculosa im Kindesalter) F. E. Struwe and O. Vollmer. *Beiträge zur Klinik der Tuberkulose und spezifischen Tuberkulose-Forschung* [*Beitr. Klin. Tuberk.*] **112**, 363–377, 1954. 40 refs.

The authors present, from the Paediatric Clinic, University of Freiburg, a detailed account of their experience in the treatment of 78 infants and children up to the age of 13 with tuberculous meningitis between 1948 and 1954, during which period different treatment regimens were used as new drugs became available. The clinical course of the disease is described in some detail. Of 73 of the children who completed treatment, 38 survived. Of 44 who were treated with streptomycin alone, 18 are alive; and of 29 treated with a combination of drugs (some given intrathecally), 20 are alive.

Among the 38 survivors, 22 have no sequelae of importance, but sequelae of moderate severity have occurred in 11 patients and grave sequelae (severe neurological and mental defects) in 5. Two children have unilateral optic atrophy and one has homonymous quadrantic hemianopia. Various degrees of hearing defect developed in 10 cases, 2 patients being totally deaf. Apart from 7 children who are mentally defective 14 others have behaviour problems.

[This is a long and carefully prepared paper, but it adds nothing new to the already voluminous literature on tuberculous meningitis.] *John Lorber*

1197. **Treatment of Tuberculous Meningitis with *iso*-Nicotinic Acid Hydrazides**

E. Appelbaum and T. A. Anderson. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **156**, 673–676, Oct. 16, 1954. 5 refs.

At the Willard Parker Hospital, New York, 10 consecutive patients with bacteriologically confirmed tuberculous meningitis were given *iso*nicotinic acid hydrazides by mouth—iproniazid to 9 and isoniazid to one—in a dosage of about 8 mg. per kg. body weight daily. No other treatment was given. There were 2 early deaths and one late death, at 5½ months; the remaining 7 patients were in good general physical condition and normal mentally over an observation period of 20 to

23 months. Optic-nerve atrophy with blindness developed in 3 patients; one of these died, in one the optic atrophy cleared up with restoration of vision, while in one vision remained severely impaired. One patient developed temporary hemiplegia; 2 had convulsions during treatment; and 4 had auditory or visual hallucinations which were attributed to the drug.

Treatment was continued for 6 to 9 months; in 3 patients there was a relapse 4 to 5 months after the cessation of treatment, but all 3 recovered after a prolonged second course of iproniazid. Resistance to iproniazid was not encountered in any of the cases.

[It is clear that *iso*nicotinic acid hydrazide treatment of tuberculous meningitis without streptomycin and without intrathecal injection is less effective than combined therapy.] *John Lorber*

PULMONARY TUBERCULOSIS

1198. **Cyanacetic Acid Hydrazide in the Treatment of Pulmonary Tuberculosis. Preliminary Observations.** (Cyanacethydrazid vid behandling av lung-tuberkulos. Preliminära iakttagelser)
N. RISKA. *Nordisk Medicin* [*Nord. Med.*] **52**, 1304–1306, Sept. 16, 1954. 2 refs.

At Nummela Sanatorium, Finland, 47 patients suffering from pulmonary tuberculosis were treated with cyanacetic acid hydrazide ("cyanazid", "reazid") in doses ranging from 3 to 12 mg. per kg. body weight for periods up to 4 months. Side-effects were observed by 23 patients; 11 complained of paraesthesiae and in 5 of these cases the treatment had to be discontinued; 10 patients complained of vertigo. A feeling of increased well-being was experienced by 24 patients, 20 were unaffected, and 3 felt worse as a result of the treatment; an average gain in weight of 2·1 kg. occurred in 20 of 28 patients treated with cyanazid alone. The amount of sputum was reduced in 13 of 25 patients, but it remained positive for tubercle bacilli in 4 of 7 patients with acute pulmonary tuberculosis and in 11 of 14 with chronic disease. The treatment had little effect upon the erythrocyte sedimentation rate or leucocyte count. Some radiological improvement was noted in 10 patients with early disease, and cavity closure occurred after 3 months' treatment in a patient who had not responded to treatment with streptomycin, isoniazid, and PAS.
D. J. Bauer

1199. **Re-treatment of Advanced Pulmonary Tuberculosis with Viomycin**
W. B. TUCKER. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **70**, 812–840, Nov., 1954. 27 refs.

A report is presented on the results of a trial of viomycin in the treatment of active pulmonary tuberculosis which was carried out in 16 hospitals of the U.S. Veterans Administration between February, 1952, and March, 1954, on a total of 125 patients. Most of the patients were suffering from advanced, progressive disease, with cavitation and positive sputum. They had all received chemotherapy in the past, and the strains of tubercle bacilli isolated showed varying degrees of resistance to streptomycin. Viomycin, injected in doses of 1 g. twice a day twice weekly, was given alone, or in combination with one or more of the following drugs: streptomycin (1 g. twice a week), isoniazid (300 mg. daily), PAS (12 g. daily), oxytetracycline (2 g. daily), and "pyrazinamide" (3 g. daily). The average duration of antimicrobial therapy was 5·7 months.

A variety of toxic manifestations was observed in 33% of cases and in 18 (14%) it was necessary to discontinue viomycin because of toxicity. The toxic effects encountered were: impairment of renal function (3 cases), severe albuminuria (1), electrolytic disturbances (2), fever (2), angioneurotic oedema (2), drug rash (3), impairment of auditory function (2), impairment of vestibular function of significant degree (2), serious nausea and vomiting (5), anaemia (1), and severe pain at the site of injection (1).

The results obtained in the series as a whole were, in approximate figures, radiological improvement in 50%, cavity closure in 25%, and sputum conversion (by culture) in 30%, with survival in 85% and arrest or inactivation of the disease in 30%. The best results were obtained when viomycin was given in combination with isoniazid, streptomycin, or PAS, but were no better than those obtained in other series in which viomycin was not used. Radiographic evidence of relapse during treatment was noted in 22% of the patients, and it was observed that such relapse was frequently associated with the development of resistance of the tubercle bacilli isolated to viomycin. The conclusion is reached that viomycin is an effective tuberculostatic drug, though less so than streptomycin or isoniazid. Moreover, the toxicity of viomycin necessitates careful laboratory control of its administration. *John Taubman*

1200. **A Five-year Assessment of Patients in a Controlled Trial of Streptomycin in Pulmonary Tuberculosis**
W. FOX, I. SUTHERLAND, and M. DANIELS. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **23**, 347–366, July, 1954. 1 fig., 13 refs.

In September, 1946, the first statistically controlled clinical trial of streptomycin in the treatment of pulmonary tuberculosis was instituted by the Tuberculosis Chemotherapy Trials Committee of the Medical Research Council. The patients were all between 15 and 30 and were suffering from acute, progressive, bilateral disease of presumably recent origin, bacteriologically proved and unsuitable for collapse therapy. They were divided at random into two similar groups, both of which were treated with rest in bed, but whereas the patients in one group were given streptomycin, 2 g. daily, for 4 months, those in the other group were not. The results after 6 months' observation showed clearly the greater benefit conferred by streptomycin over this period. In the present report the progress of the two series of patients over a period of 5 years is compared in order to determine the long-term effects of this treatment.

Of the 107 patients admitted to the trial, 55 were given streptomycin and 52 were not. After the initial 6-month period, treatment in individual cases was decided

without reference to the investigation. In fact, however, both chemotherapy (with streptomycin or other drugs) and collapse therapy were used to a limited and similar extent in the two groups. During the first 18 months there was a high mortality among the patients in the control group, 14 (27%) of whom died in the first 6 months, 22 (42%) by the end of a year, and 30 (58%) within 18 months. After this, mortality in this group was much lower, and at the end of 5 years 17 (33%) were still alive. In the group treated with streptomycin mortality was considerably less than in the control group during the first 18 months, only 4 (7%) of the patients dying within the first 6 months and 19 (35%) in 18 months. Unlike the control series, however, there was no subsequent decline in mortality, so that at the end of 5 years only 23 (42%) of the patients were still alive. The difference between the two series at the end of 5 years, although still significant, is thus less than was to be expected from the early results. At the end of 2 years the disease was classified as "quiescent" in 19 (61%) of the 31 survivors of the series treated with streptomycin, and in 6 (30%) of the 20 survivors of the control series. By the end of 5 years the disease was classified as "arrested" in 13 (57%) of the 23 surviving patients of the former series and in 5 (29%) of the 17 survivors of the latter.

On relating the mortality in both groups to the initial clinical condition and to the initial response to treatment it appeared that cavitation and pyrexia on admission were associated with an adverse prognosis, and this was also true of failure to show radiological improvement in the first 4 months. The prognosis was also related to the bacteriological response to treatment, being good among those cases in which the sputum was negative on culture at the end of 4 months, and poor among those in which tubercle bacilli were found on direct examination at this time. On the other hand high degrees of drug resistance were not always associated with a poor prognosis.

[This clearly documented report is of major interest, being concerned with the only investigation into the long-term efficacy of streptomycin which has so far been carried out with adequate controls. The authors point out that whereas the inclusion of the control series was, at the time, "ethically justified by the very limited supplies of streptomycin", the advent of effective chemotherapy makes it unlikely that any similar controls will ever be available again, and for this reason the detailed study of a group of young people with progressive bilateral pulmonary tuberculosis treated without chemotherapy is in itself of great value.] *T. M. Pollock*

1201. **Early Ambulatory Treatment of Pulmonary Tuberculosis with Isoniazid**

M. BUNDY, G. E. MARTIN, I. H. ALEXANDER, and C. C. KUEHN. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **44**, 1027–1037, Aug., 1954. 6 refs.

Concerned about the long waiting list for admission to the City Tuberculosis Hospital, Pittsburgh, where the average duration of stay was 13 months, the authors in June, 1952, began to discharge patients earlier than usual —that is, after sputum culture had been negative for 2 consecutive months, the patient being examined thereafter in the out-patient department at monthly intervals. Of 315 patients discharged from the hospital between June 1, 1952, and March 31, 1953, 172 continued to receive treatment as out-patients, 111 with isoniazid alone and 61 with streptomycin and PAS. Most of these patients on admission to hospital had advanced pulmonary tuberculosis, but their condition had improved at the time of discharge. Of the patients treated with isoniazid 38 (34%) were in hospital 8 months or less and 58 (52%) were in hospital 11 months or less; of the patients treated with streptomycin and PAS 31 (50%) were discharged within 8 months and 41 (67%) within 11 months.

During the follow-up period of 17 months 3 of the patients receiving isoniazid and 4 of those receiving streptomycin and PAS had to be readmitted to hospital, a failure rate of 4%. This compares with the average readmission rate for the hospital of 32% of admissions in one year. The authors state that in a few cases after discharge sputum culture was positive, but unless the radiological and clinical findings substantiated this it was their practice to wait until a third positive sputum culture was obtained before readmitting the patient to hospital.

[In Britain the disease in many of these cases would not be regarded as quiescent, and the paper indicates, if anything, only that such patients can be kept in a reasonable state of health by domiciliary antibiotic treatment.] *G. M. Little*

1202. **Adrenal Cortical Function during Isoniazid Therapy for Pulmonary Tuberculosis**

T. F. FRAWLEY and P. J. ROSCH. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **70**, 841–851, Nov., 1954. 40 refs.

The authors point out that in patients with pulmonary tuberculosis treated with isoniazid the frequent occurrence of defervescence, increased appetite, weight gain, and euphoria out of proportion to the objective improvement is strongly reminiscent of the effects of administration of corticotrophin (ACTH) and cortisone. This suggests the possibility of adrenal cortical stimulation as either a primary effect of isoniazid or a secondary consequence of its action. Working at Albany Hospital (Albany Medical College), New York, they therefore carried out studies of adrenal function before and during isoniazid therapy on 8 tuberculous patients selected at random. The status of the disease in all 8 patients was approximately the same, and throughout the period of study they were treated with rest and nutritious diet, but were given no specific treatment apart from isoniazid, which they received in doses of 3 to 5 mg. per kg. body weight daily for 4 to 20 weeks.

Before and at intervals during treatment adrenal cortical activity was assessed from determinations of the eosinophil count and of urinary 17-ketosteroid, uric acid, creatinine, and 17-hydroxycorticoid excretion, and cortical responsiveness was assessed by means of the 8-hour intravenous corticotrophin test. In no case was any significant or constant deviation from the normal level

of adrenal function observed, although all patients reported some improvement in mood and other non-specific effects, in addition to varying degrees of objective improvement.

The authors discuss at some length the possible endocrine factors involved in pulmonary tuberculosis, and examine critically the limitations of the present study. In concluding that the euphoria induced by isoniazid must be due to some action on the central nervous system rather than on the adrenal cortex, they point out that evidence of such action has been provided by animal experiments and by reports of psychosis occurring as a result of isoniazid therapy.

[Since this investigation is not likely to be repeated, in view of the present tendency to give multiple drug therapy, the information obtained concerning the extra-chemotherapeutic action of isoniazid is of some value.]

John Taubman

1203. **Isoniazid in the Treatment of Tuberculosis Complicated by Diabetes.** (Isonicotinsäurehydrazid in der Behandlung der Diabetikertuberkulose)
K. J. Irskens. *Beiträge zur Klinik der Tuberkulose und spezifischen Tuberkulose-Forschung* [*Beitr. Klin. Tuberk.*] **112**, 335–345, 1954. 8 figs., 38 refs.

The author reports, from the Auguste-Victoria Sanatorium, Bad Lippspringe, Germany, that the carbohydrate tolerance of 20 out of 58 diabetic women decreased considerably while they were receiving treatment with isoniazid for pulmonary tuberculosis. In all but one case, however, this deterioration in the diabetic state was temporary and was reversed when isoniazid was discontinued. In a few cases intravenous injections of a preparation of vitamin-B complex improved the carbohydrate tolerance during isoniazid treatment, but it was shown that of the individual members of the complex only pyridoxine was effective.

No evidence is offered regarding the mode of action of isoniazid on disordered carbohydrate metabolism, but several theoretical possibilities are discussed. In view of the possible danger involved the author warns against the domiciliary treatment with isoniazid of diabetic patients with tuberculosis. *John Lorber*

1204. **The Treatment of Coexisting Addison's Disease and Active Pulmonary Tuberculosis**
J. S. L. Browne, M. Aronovitch, J. C. Beck, W. Leith, and J. F. Meakins. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **228**, 491–505, Nov., 1954. 7 figs., 16 refs.

Before the introduction of cortisone the prognosis in cases of Addison's disease with active pulmonary tuberculosis was poor. The authors describe the treatment and management of 5 such cases seen recently at the Royal Victoria Hospital, Montreal. The maintenance dose of cortisone was 12·5 to 37·5 mg. daily. In 4 of the cases the pulmonary lesions were treated with 1 g. of streptomycin 3 times a week and 12 g. of PAS daily; in the fifth case, that of an out-patient, isoniazid ("rimifon") was given for 4 months, followed by streptomycin and PAS.

In at least 2 of the cases the lesions in the lung appeared to improve more rapidly when all three drugs were being taken than when streptomycin and PAS were given alone. One patient received cortisone for 2 years without any tuberculostatics, and at no time was there an extension of the pulmonary lesion. All the patients remained well for 1 to 3½ years after the administration of antituberculous drugs ceased, treatment with cortisone and sodium chloride being continued; 4 of the patients are actively employed.

The authors emphasize that only a maintenance dose of cortisone is required once the "crises" have been successfully overcome. The paper contains several reproductions of radiographs together with a detailed clinical history of each case. *Paul B. Woolley*

1205. **"Ventilatory" and "Effective" Respiratory Function after Therapeutic Collapse Procedures.** ("Ventilatorische" und "effektive" respiratorische Funktion nach kollapstherapeutischen Eingriffen)
C. W. Hertz. *Thoraxchirurgie* [*Thoraxchirurgie*] **2**, 216–249, Oct., 1954. 7 figs., bibliography.

In this paper from Tönsheide Hospital, Holstein, the author describes an investigation of the changes in pulmonary function of 72 patients after collapse therapy. He considers that pulmonary function can be divided into "ventilatory" function, which is defined as the result of mechanical lung action and is measurable by spirometry, and "effective" function, which is a measure of the efficacy of respiration and can be determined by blood-gas analysis. In the present series spirometry, bronchospirometry, and estimations of blood concentration of oxygen, carbon dioxide, and haemoglobin were carried out in all cases. The results are presented in tabular form,

On the basis of his findings the author suggests that the effect of collapse therapy on pulmonary function is of three types. (1) There may be a parallel reduction of both ventilatory and effective function. In these cases blood perfusing the collapsed area of lung is not adequately oxygenated and, on mixing in the pulmonary veins with blood from the uncollapsed parts of the lungs, reduces the mean total blood oxygen saturation. (2) In a larger number of cases pulmonary ventilation is noticeably reduced but arterial oxygen saturation is normal or nearly so. The explanation may be that the alveoli of the non-collapsed area of the lung provide an adequate oxygen concentration, as in some cases of pneumothorax, or else, as in some cases of thoracoplasty, that the blood supply to the collapsed area is diminished so that there is no great shunt of systemic venous blood into the pulmonary veins. (3) There may be good ventilatory function but distinct hypoxaemia, especially after phrenic crush. In these cases the absence of hemidiaphragmatic action may be compensated for by a deeper excursion of the other half or by tachypnoea, but there is a very large area of collapse containing numerous inadequately aerated alveoli to which the blood supply nevertheless remains normal. This was demonstrated by the author in a few cases in which sudden blocking of a major bronchus was produced,

whereupon the lack of oxygen supply in the dependent part of the lung resulted in a decrease of arterial oxygen saturation.

The author concludes that "effective" respiratory function is the resultant of ventilatory efforts on the one hand and the state of the pulmonary circulation on the other, and can be studied adequately only by a combination of spirometry and blood gas analysis.

D. Goldman

1206. **Partial Resection for Pulmonary Tuberculosis. 100 Cases Analysed**

R. S. FRANCIS. *Tubercle* [*Tubercle* (*Lond.*)] **35**, 238–244, Oct., 1954. 1 ref.

The author analyses the first 100 cases of partial resection for pulmonary tuberculosis carried out at Harefield Hospital, Middlesex, between 1947 and 1951. In 71 cases lobectomy was performed, in 10 lobectomy and segmental resection, and in 19 segmental resection only. The end-results were satisfactory in 73 cases, although 9 of these required further treatment. In 34 cases the disease took the form of large, round foci 3 cm. or more in diameter, and in 31 (90%) of these there were good end-results (2 requiring further treatment); no fistulae or deaths occurred in this group. Of the 66 other cases, in which the disease took various forms, bronchial fistulae occurred in 13; in this group there were 4 operative deaths (one from anoxia, 2 due to fistula and spread of the infection, and one from air embolism at pneumoperitoneum refill), and 5 late deaths (4 due to fistula and extension of the disease and one to cor pulmonale).

The series was also analysed in respect of the type of lesion and other factors. No relationship was found between the duration of the disease and the result of resection. Bad prognostic factors were inadequate preoperative chemotherapy (particularly streptomycin), tuberculous disease elsewhere in the body, inexact demarcation of the extent of the disease, endobronchitis, sputum positive for tubercle bacilli, and accidental opening of a friable cavity at operation. Where breakdown occurred it usually did so within 18 months of operation. Ipsilateral re-activation of the disease after upper lobectomy occurred much more frequently when thoracoplasty was not carried out; it is now standard practice at this hospital to perform thoracoplasty about 2 weeks after resection. In the later years of the period the more effective use of chemotherapy and other measures designed to reduce the activity of the disease preoperatively have given improved results and a considerable reduction in the incidence of fistula.

F. J. Sambrook Gowar

1207. **The Surgical Treatment of Pulmonary Tuberculosis—before and after the Introduction of Antibiotics and Chemotherapeutics**

C. SEMB. *Journal of the Oslo City Hospitals* [*J. Oslo City Hosp.*] **4**, 123–150, Sept.–Oct., 1954. 6 figs.

An analysis is presented of all cases of pulmonary tuberculosis treated surgically at Vardåsen Sanatorium and Ullevål Hospital, Oslo, between 1932 and 1954, the total of 2,064 cases being divided into (1) 1,053 cases treated between 1932 and 1948, before the advent of streptomycin, and (2) 1,011 cases treated between 1949 and 1953, after streptomycin had become available. The average number operated on each year has thus more than trebled since the introduction of streptomycin, mainly as a result of the inclusion of cases with active and extensive disease which would previously have been unsuitable for surgery. Preliminary treatment with antibiotics is used sparingly to avoid drug resistance, being limited so far as possible to a short course starting 8 to 10 days before the operation. Long-term intermittent chemotherapy is used, however, in advanced cases and frequently brings them within the scope of surgery.

Temporary collapse, especially by artificial pneumothorax, is used only for small productive lesions in uncomplicated cases. A small thoracoplasty is considered to be superior to extrapleural pneumothorax except in certain cases with paralysis of the diaphragm and in children, where thoracoplasty would cause a severe scoliosis. Plombage has not been used, and phrenic paralysis has been employed to a very limited extent, mainly combined with pneumoperitoneum in the treatment of basal cavities.

In the author's opinion thoracoplasty with extrafascial apicolysis remains the treatment of choice for lesions in the upper and posterior parts of the lung. Since the introduction of the modern antibiotics resection of only 4 to 6 ribs is sufficient in 90% of cases. Thoracoplasty is also indicated in the presence of total and subtotal destructive lesions, secondary pneumonectomy being then better tolerated if it becomes necessary. In Group 1 972 patients were treated by this method, and in Group 2 411. In the latter group the operative mortality was 2%, and 81% were cured. Bilateral thoracoplasty was performed in 19 cases in Group 1 and in 52 in Group 2, the mortality falling from 16% in the former to 4% in the latter and the cure rate rising from 42% to 73%.

Resection is used mainly as a supplementary treatment in cases where collapse therapy has failed or is contraindicated by the position or nature of the lesion. In the whole series 275 resections of all types were performed with an operative mortality of 3·6% and a late mortality of 5·1%; 77·8% of the patients were rendered sputum-negative. The end-results of segmental resection have been less favourable than those of other types of resection owing to spread occurring in the same or contralateral lung. [Complete figures for bronchial fistula are not given.]

For tuberculous empyema, thoracoplasty with extrafascial apicolysis is again regarded as the treatment of choice. Decortication is carried out only where no active foci are demonstrable in the lungs, while in cases of apical disease thoracoplasty is first performed, followed by decortication 3 to 4 months later. There were 74 cases of tuberculous empyema in Group 1, 55 of which were treated by thoracoplasty with 7 operative deaths and a cure rate of only 40%. In Group 2 there were 68 cases of tuberculous empyema, of which 54 were treated by thoracoplasty (13 with secondary resection) and 14 by primary resection, with an operative mortality of 3% and a cure rate of 72%.

F. J. Sambrook Gowar

Venereal Diseases

1208. **On the Clinical and Pathological Aspects of Chronic Benign Plasma-cell Balanoposthitis.** (Zur Klinik und Histologie der Balanoposthitis chronica circumscripta benigna plasmacellularis-Zoon)

F. NÖDL. *Archiv für Dermatologie und Syphilis* [*Arch. Derm. Syph. (Berl.)*] **198**, 557–566, 1954. 4 figs., 14 refs.

Chronic benign circumscribed plasma-cell balanoposthitis was first described as a clinical entity by Zoon in 1952 (*Dermatologica (Basel)*, **105**, 1; *Abstracts of World Medicine*, 1953, **13**, 52). References to it in the literature are infrequent and the author believes that it is often confused with the erythroplasia of Queyrat, but many cases are probably never seen medically. Biopsy and histological examination formerly provided the only certain method of diagnosis. He then describes a case, seen at the University Skin Clinic, Göttingen, of a 62-year-old man who had developed a red patch on the glans and inner side of the prepuce one year previously. The lesion was at first diagnosed as erythroplasia and *x*-ray treatment given, but later biopsy did not confirm the diagnosis. The author describes in great detail the clinical appearances of the lesion, and discusses the differential diagnosis from chemical dermatitis, balanitis xerotica obliterans, and balanitis due to syphilis, gonorrhoea, diphtheria, or fungi. Only the erythroplasia of Queyrat is considered to present differential diagnostic difficulties.

The histological picture found at biopsy is described and illustrated in photomicrographs. The most important characteristics were the deposit of quantities of haemosiderin which gave a positive Turnbull-blue reaction and a profound infiltration of the tissues with plasma cells, together with changes in the walls of the small blood vessels. The lesion improved under treatment with tannin powder and boracic and zinc ointments. The author, differing from Zoon, claims that it is possible to differentiate this lesion on clinical grounds alone; he considers the essential pathological process to be a disturbance of the circulation and permeability of the local capillaries.

R. D. Catterall

1209. **Observations on the Applied Epidemiology of Gonorrhoea**

D. O. ANDERSON and A. J. NELSON. *Canadian Journal of Public Health* [*Canad. J. publ. Hlth*] **45**, 381–391, Sept., 1954. 2 figs., 2 refs.

In the Province of British Columbia between 1946 and 1953 the number of reported cases of infectious syphilis fell by 97%, whereas the corresponding figure for gonorrhoea was only 36%. Gonorrhoea, therefore, is now considered the major problem in the control of venereal disease. In this paper from the British Columbia Department of Health and Welfare, Vancouver, the authors review present and past thinking regarding the epidemiology of gonorrhoea and describe a recently introduced control programme for the City of Vancouver which is based on the fact that a large number of the male cases seen were most probably the result of contact with a comparatively small number of infected women who either did not know they had gonorrhoea or made no effort to have it treated and thus formed a reservoir of infection sometimes for indefinite periods. A successful epidemiological attack must therefore be based on the recognition and elimination of this reservoir. In essence, this means that the infected, untreated women must be identified through their recent male contacts and brought to treatment in as short a time as possible if the best results are to be achieved.

Arising from these considerations a four-point programme has been instituted, as follows. (1) Intensive interviewing of all males coming for treatment regarding their female contacts during the 6-day period preceding the onset of symptoms. (2) Attempts made to locate all identifiable female contacts within 24 to 48 hours. (3) Immediate treatment for gonorrhoea, irrespective of bacteriological findings, of all female contacts located. (4) An effort made to enlist the cooperation of proprietors and managers of so-called hotels in the city where many of the promiscuous contacts take place. The results of this programme, after 6 months of operation, are considered encouraging but since 42% of all patients with venereal disease in this area are first seen by a private physician, the enlistment of his cooperation too in the tracing of contacts is an urgent necessity.

Benjamin Schwartz

1210. **Skin Tests for Lymphogranuloma Venereum in Non-specific Urethritis.** [In English]

R. R. WILLCOX. *Acta dermato-venereologica* [*Acta derm.-venereol. (Stockh.)*] **34**, 430–438, 1954. 1 fig., 2 refs.

This paper forms part of a series describing an investigation to ascertain whether patients suffering from so-called non-specific urethritis react to the antigens of viruses of the lymphogranuloma–psittacosis group. [One of the series has already been published (Macrae and Willcox, *Brit. J. vener. Dis.*, 1953, **29**, 231; *Abstracts of World Medicine*, 1954, **15**, 475); a second is in the press.] In the present paper the author describes the results of the Frei test, carried out at St. Mary's Hospital, London, or King Edward VII Hospital, Windsor, on 84 patients suffering from non-specific genital infections and 62 controls attending the venereal disease clinics for other reasons. Two preparations of antigen were used —a vaccine made in Britain and a commercial product, "lygranum", made in the United States. The results of the tests were read at 48 hours, a positive result being recorded when an inflammatory papule more than 6 mm. in diameter developed on the test arm but not on the control arm. A papule 5 to 6 mm. in diameter was inter-

preted as a " doubtful " positive reaction, and a papule less than this in diameter as a negative reaction. The results appeared to be similar with the two vaccines. Positive reactions were obtained in 13·1% of cases of " non-specific " infection compared with 4·8% of the controls. In the former group there did not appear to be any relationship between the incidence of positive and doubtful reactions and activity or duration of the infection. It was concluded that it was not possible to establish any relationship between " non-specific " genital infection and reactivity to Frei antigen. *A. J. King*

SYPHILIS

1211. **The Treponemal Immobilization (T.P.I.) Test of Nelson. Its Importance in the Diagnosis and Understanding of Human Syphilis as Judged from Personal Experience.** (La prueba de inmovilización treponémica de Nelson (T.P.I.). Su interés diagnóstico y doctrinal en la sífilis humana, seguida de un comentario derivado de nuestra experiencia personal)

X. VILANOVA. *Actas dermo-sifiliográficas* [*Act. dermo-sifiliogr. (Madr.)*] **46**, 3–24, Oct., 1954. 4 figs.

The author reviews the development of serological tests for syphilis, including the treponemal immobilization (T.P.I.) test of Nelson and Mayer, and discusses the results obtained with this test during the past 18 months in the School of Dermatology of the University of Barcelona.

The value of the test was confirmed, although it was found to be less sensitive than the standard serological tests in cases of early secondary syphilis, the reaction being negative in 11 out of 31 such cases. On the other hand in a series of 29 cases of neurosyphilis the T.P.I. reaction was positive in the blood in every case in which the cerebrospinal fluid showed specific change, a finding of particular value in that it will enable lumbar puncture to be avoided in many cases. Amongst his other conclusions the author considers that a negative T.P.I. reaction rules out the presence of syphilis (or other treponematosis) except in the case of infections of less than 3 months' duration or congenital disease in an infant of less than 3 months. In treated syphilitics negativity of the T.P.I. reaction, together with the other clinical findings, is an important factor in the determination of cure.

[No references are given to the many authorities cited in the text.] *Eric Dunlop*

1212. ***Treponema pallidum* Immobilization Test in the Evaluation of Patients with Positive Serologic Tests for Syphilis**

A. B. KERN. *New England Journal of Medicine* [*New Engl. J. Med.*] **251**, 807–810, Nov. 11, 1954. 5 refs.

Writing from the U.S. National Naval Medical Center, Bethesda, Maryland, the author makes a plea for the wider use of the treponemal immobilization (T.P.I.) test, pointing out the potential danger to the patient's future of failure to diagnose syphilis because of a negative result of the more common reagin tests, or on the other hand the unnecessary hardship which may be caused by accepting a biologically false positive reaction as evidence of syphilitic infection. Brief histories of 17 typical cases in which the T.P.I. test confirmed or refuted a doubtful diagnosis of syphilis are presented.

The immobilizing antibody occurs only in syphilis and closely related treponemal infections, namely, yaws, bejel, and pinta. It usually lags behind reagin in appearance and disappearance; it may not appear in early cases which have been adequately treated, and it usually does not disappear from the serum in long-standing cases, whether treated or not. Thus it may give a false negative result in an early case; on the other hand a positive test result—like the Mantoux reaction in tuberculosis—shows only that the patient has had a syphilitic infection at some time. The progress of the disease must then be judged from the clinical course and from repeated quantitative reagin tests; a positive T.P.I. reaction does not necessarily indicate the need for treatment. The immobilization test is of most use in the differentiation between false positive reagin-test results and latent syphilis. It is valuable also in that it remains positive in untreated cases of neurosyphilis, cardiovascular and congenital syphilis, and of gumma. Unfortunately the test is complicated and difficult to perform, requires expensive materials and trained personnel, and to the author's knowledge is at present carried out at only eleven laboratories in the United States (a list of these is given). It is urged in conclusion that this useful test should be made more widely available.

Ferdinand Hillman

1213. **The Specificity of the Treponemal Immobilization Test**

H. E. ZELLMANN. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **38**, 506–521, Nov., 1954. 14 refs.

The *Treponema pallidum* immobilization (T.P.I.) test was carried out at Johns Hopkins Hospital, Baltimore, on 45 normal persons and on 110 patients with diseases other than syphilis. Apart from 4 cases in which the test was " unsatisfactory ", all the results were negative except for a doubtful reaction in a case of disseminated sclerosis and a positive reaction in a case of paroxysmal auricular fibrillation. Neither of these patients showed any other evidence of syphilis, and the results of the standard tests for syphilis (S.T.S.) were negative in both instances. As it was not possible to obtain second specimens of serum for confirmation it is not known whether these were false positive reactions or resulted from errors in technique. These cases, together with others reported in the literature, give a total of one doubtful and 3 positive reactions to the T.P.I. test among 1,397 presumed non-syphilitic sera tested, representing a possible incidence of non-specific reactions of 0·3%.

Further tests were carried out on sera from 441 patients with clinically verified syphilis drawn from private practice who had been treated by various methods 1 to 40 years previously. The T.P.I. reaction was positive in 24 and negative in 44 cases of treated early syphilis, and positive in 351 out of 372 patients with treated late

symptomatic syphilis. The T.P.I.-negative cases in this group included patients with tabes (5), other forms of neurosyphilis (5), and late congenital syphilis (3). It is therefore concluded that in treated late syphilis, with very few exceptions, the immobilizing antibody, unlike reagin, persists in the serum indefinitely regardless of the antisyphilitic treatment given, whereas in treated early syphilis it may disappear. The immobilizing antibody similarly persists in treated congenital syphilis, and although its behaviour in latent syphilis has not been studied, it is reasonable to suppose that it persists also in cases of late latent syphilis (of more than 4 years' duration) despite treatment. It is therefore considered that provided treated early syphilis can be excluded and there is no clinical evidence of late syphilis (especially tabes and congenital syphilis) a negative T.P.I. reaction, confirmed by repetition on the same specimen of serum, can be used to differentiate between syphilitic infection and the biological false positive phenomenon, regardless of any treatment which may have been given.

[This paper gives a most useful survey of the results of T.P.I. tests at various stages of syphilis gathered from the principal series so far reported in the literature.]

A. E. Wilkinson

1214. **Frozen Syphilomatous Rabbit Testes as Source of *Treponema pallidum* for the Immobilization (TPI) Test for Syphilis**

R. I. ANDERSON, J. F. KENT, and R. W. SANDERS. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **38**, 527–530, Nov., 1954. 3 refs.

This report from the Walter Reed Army Medical Center, Washington, D.C., extends the observations of Chorpenning *et al.* (*Amer. J. Syph.*, 1952, **36**, 401; *Abstracts of World Medicine*, 1953, **13**, 113) who used syphilomatous rabbit testes kept at −55° to −45° C. as a source of treponemes in the treponemal immobilization (T.P.I.) test. A total of 185 testes were collected and stored in the frozen state for varying periods—91 for 1 to 7 days, 83 for 1 to 12 weeks, and 11 for 3 to 18 months. On thawing and extraction with the basal medium used in the test the average motility of the organisms was 90%, while the average motility of treponemes extracted from 198 unfrozen testes was 97%. The suspensions from the frozen testes were uniformly satisfactory when incubated under test conditions (18 hours at 35° C.). The proportion of motile organisms recovered from the testes stored for the maximum period of 18 months was little different from that from testes stored for short periods, and the slightly lower motility compared with that of treponemes from fresh testes appears to be related to damage inseparable from the processes of freezing and thawing rather than to the duration of storage in the frozen state.

By means of a special container refrigerated by solid carbon dioxide, frozen syphilomatous testes have been sent by air mail to centres as far from Washington as Germany and Cuba. On receipt, treponemes from these testes have been successfully used to establish syphilitic infection in rabbits.

A. E. Wilkinson

1215. **The Agglutination of Pathogenic *Treponema pallidum* by Syphilitic Serum.** (Sulla reazione di agglutinazione fra siero di sifilitico e *Treponema pallido* patogeno)

L. DARDANONI. *Rivista dell'Istituto sieroterapico Italiano* [*Riv. Ist. sieroter. Ital.*] **29**, 440–456, Sept.–Oct., 1954. 6 figs., 20 refs.

After a brief review of the literature concerning antitreponemal antibodies, the author describes his experience at the Institute of Hygiene of the University of Palermo with the *Treponema pallidum* agglutination test as performed by the technique of McLeod and Magnuson (*Publ. Hlth Rep.* (*Wash.*), 1953, **68**, 747; *Abstracts of World Medicine*, 1954, **15**, 212). It is assumed that the treponemal agglutinating antibody in syphilitic serum is identical with the immobilizing antibody of Nelson.

The rabbits used for testicular culture were given a dose of *x* rays on the day before inoculation, and fresh bovine serum was used as conglutinin. Sera from 2 healthy subjects and 6 patients with syphilis were used, one of the latter, from a patient with a gumma, giving a negative response to the immobilization (T.P.I.) test of Nelson and a weak positive result with the agglutination test. The procedure is described, and photographs are reproduced to show negative and positive agglutination and to illustrate the annotation used (+ to ++++) for recording the results, both the presence of clumps and the absence of free treponemes being used as indices of positivity.

The results proved difficult to read—only in control tests in which both the patient's serum and the bovine serum were replaced by saline was there no agglutination at all, an increase in the size of the agglutinate was not always associated with a decrease in the number of free single treponemes, and positive sera produced some agglutination even in the absence of complement. The use of an initial suspension of 90 treponemes per dark field (as opposed to 30 in the original technique) made no material difference to the results.

It is concluded that since the occurrence of autoagglutination in the treponemal suspension makes both qualitative and quantitative evaluation of the results uncertain, the treponemal agglutination test, which is delicate and costly to carry out, has not yet reached a sufficiently mature stage of development to warrant its use as a substitute for the T.P.I. test.

Ferdinand Hillman

1216. **The Results of Treatment of Syphilis with Penicillin alone.** (Ergebnisse alleiniger Penicillinbehandlung der Lues)

R. HAENSCH. *Hautarzt* [*Hautarzt*] **5**, 470–472, Oct., 1954.

The author reports the clinical and serological results of a 3-year follow-up study of 174 patients with secondary and tertiary syphilis treated at the Municipal Skin Clinic, Wuppertal, Germany. In 37 cases the patient had had no previous treatment, while the remaining 137 had been treated with a combination of arsenic and bismuth.

Out of 16 patients with secondary syphilis, who were given a total dose of either 6 or 9 mega units of a depot

preparation of penicillin in doses of 400,000 or 600,000 units daily, 15 became seronegative and remained so for 3 years. No case of clinical or serological relapse occurred in this group. Of 17 patients with latent syphilis treated with a total of 6 mega units of penicillin, 5 defaulted immediately, 10 were followed up over a period of 2 years, and 8 for 3 years. The author had the impression [based apparently on serological tests] that the dose of 6 mega units was too small, and most of the patients in this group were therefore given further doses totalling 9 mega units 6 months later, making 15 mega units in all. In the serological tests titres were not determined, the results being reported merely as positive, doubtful positive, and negative. Of the 8 patients observed up to 3 years, 3 showed clinical improvement and 5 were seronegative. One of these patients relapsed serologically one year after treatment, but after further penicillin treatment became seronegative and remained so for the remaining 2 years of observation.

[The group of 137 patients who had previously received arsenic and bismuth is of little interest because the stage of their disease is not specified, although a vague statement is made that most of them were in the secondary stage when treatment with heavy metals was begun. The exact doses of these, however, are not given. The author claims that his results agree in general with those reported in the American and German literature.]

R. D. Catterall

1217. **Topical Cortisone in the Treatment of Syphilitic Interstitial Keratitis. Preliminary Report of 20 Cases (26 Eyes)**

G. O. HORNE. *British Journal of Ophthalmology* [*Brit. J. Ophthal.*] **38**, 669–672, Nov., 1954. 5 refs.

To emphasize the value of the topical application of cortisone in syphilitic interstitial keratitis the author describes 20 cases (26 eyes) so treated at the General Infirmary at Leeds. He states that the three principal criteria on which assessment of results should be based are: (1) immediate effect on inflammation ; (2) duration of individual attacks and incidence of relapses; and (3) the final visual acuity. Drops of a suspension of cortisone acetate (5 mg. per ml.) were given to all the patients, who received at the same time systemic treatment for syphilis—penicillin, with or without bismuth. The observation period was over a year in the majority of cases.

There was rapid relief of symptoms with restoration of normal vision in nearly all the cases. In some the improvement was slower, the rate being influenced by the duration of the disease before treatment started and by the dosage of cortisone. Adequate dosage appeared to shorten attacks. Relapses were well controlled, but the author considers the series too small and the period of observation too short for assessment of the frequency of relapses. Final visual acuity in this series was considered to be much superior to that obtained in other reported series; in only 3 eyes was visual acuity less than 6/12. No contraindication to the use of cortisone was noted.

[The author does not define an " adequate dosage " of cortisone; nor does he emphasize sufficiently that in the long-standing case cortisone may act much more slowly and cannot be expected to remove established fibrosis. A more detailed report, which is promised, should be valuable.]

Robert Lees

1218. **The Treatment of Syphilitic Meningitis.** (Die Behandlung luischer Meningitiden)

W. GRÜTER and H. EHRHARDT. *Münchener medizinische Wochenschrift* [*Münch. med. Wschr.*] **96**, 1343–1347, Nov. 12, 1954. 3 figs., bibliography.

The authors review the present position regarding the treatment of syphilitic meningitis in the light of their own experience at the University Neurological Clinic, Marburg, and of reports in the literature. Briefly, they conclude that penicillin is superior to the older methods of treatment with metallic salts. The minimum total dose of penicillin recommended is 9 to 10 mega units, and this is best given in single intramuscular injections of 600,000 units of depot penicillin daily. If the condition of the patient permits, a few injections of bismuth should precede the administration of penicillin in order to avoid the Herxheimer reaction. In their view additional fever therapy is not advisable as it introduces dangers of its own without materially benefiting the patient. If the cerebrospinal fluid shows evidence of inflammatory changes within 6 to 9 months after the initial treatment a further similar course of penicillin is given. As an alternative, in the rare cases which are allergic or resistant to penicillin, the older metallotherapy, together with a broad-spectrum antibiotic such as aureomycin, is recommended. Three representative case histories are given.

G. W. Csonka

1219. **Early Syphilitic Hepatitis**

R. V. RAJAM and P. N. RANGIAH. *Indian Journal of Venereal Diseases and Dermatology* [*Indian J. vener. Dis.*] **20**, 83–94, July–Sept., 1954. 3 figs., 13 refs.

It is considered logical to assume that in early syphilis the liver will be invaded by *Treponema pallidum* in vast numbers, which may result in clinical or " sub-threshold " asymptomatic hepatitis. The literature contains few references to the changes in the liver in the early stages of syphilis, but the authors cite the finding by Hausman of multiple, diffuse, interacinar, miliary granulomata, and that by Wagner *et al.* of abnormal zinc sulphate turbidity reactions. In a few cases there is clinical evidence of hepatic dysfunction, with enlargement of the organ and jaundice. The estimated incidence of clinically manifest early syphilitic hepatitis is variable but low, being less than 1%.

The authors discuss three types of early syphilitic disease of the liver—early acute benign hepatitis, " hepato-recurrence ", and chronic interstitial pericellular cirrhosis of prenatal infantile syphilis—and describe 3 cases representative of each of the three types.

It is suggested that routine needle biopsy of the liver and liver function tests in early syphilis would provide information on the frequency of asymptomatic hepatic damage.

Douglas J. Campbell

Tropical Medicine

1220. **A Comparative Study of Fumagillin and Oxytetracycline in Amebiasis**
J. H. KILLOUGH and G. B. MAGILL. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] 3, 999–1007, Nov., 1954. 11 refs.

The authors' preliminary report on the results of treatment of amoebiasis with fumagillin has already been published (*Science*, 1952, **115**, 71; *Abstracts of World Medicine*, 1952, **12**, 103). They now report their results in a larger series of cases.

Fumagillin, in a dosage of 5 to 200 mg. daily for 14 days, was given to 67 adult males with proved infection with *Entamoeba histolytica*. For purposes of comparison 48 similar patients (16 of whom had amoebic dysentery) were treated with oxytetracycline in a dosage of 2 g. a day for 2 to 6 weeks. All patients were afterwards observed in hospital for 4 weeks, and later recalled for examination at intervals up to 24 months.

Of the patients treated with fumagillin 13 had dysentery, and in 11 of these the symptoms disappeared after 9 to 14 days' treatment. In the remaining 2 the signs of hepatic abscess developed; one of these patients died, the other responded slowly to administration of oxytetracycline with chloroquine. In 12 of the patients in this group the initial response was rapid, the stools being free from amoebae in 3 days; in 7 of these, however, amoebae recurred within 6 months of cessation of treatment. Oxytetracycline was given to 16 patients with dysentery, and in 12 of these there was a symptomatic response in 2 to 14 days. One patient continued to have abdominal cramp until one week after the termination of treatment, while 3 developed a hepatic abscess; 2 of the latter died. Of the 14 surviving patients, 8 later had a recurrence of amoebae in the stools without symptoms.

Fumagillin was given to 54 patients without dysentery; in 51 the stools became negative for amoebae within 3 days and in 3 within 96 hours. Excluding patients who had received inadequate dosage (less than 50 mg. a day) the recurrence rate was 38%. The response was similar in 32 patients without dysentery who were given oxytetracycline, but the recurrence rate was about 45%.

The chief toxic effects of fumagillin were anorexia, beginning on the second or third day of treatment, and loss of weight. Some patients complained of nausea and vomiting. Dermatitis developed in about one-quarter of the patients, lesions appearing on the face, neck, hands, feet, chest, and abdomen between the 4th and 12th days of treatment. The lesions were symmetrical in distribution and covered large areas; they subsided within a week of cessation of treatment.

It is concluded that fumagillin and oxytetracycline are about equally effective in patients without dysentery, though neither drug has any effect upon hepatic abscess if present. The optimum dose of fumagillin is 50 mg. a day; larger doses cause anorexia, while with smaller doses relapse occurs. Fumagillin should be reserved for chronic, drug-resistant, intestinal amoebiasis; it is not suitable for routine clinical use.

F. Hawking

1221. **Studies on Schistosomiasis. X. Comparison of Stool Examination, Skin Test, Rectal Biopsy, and Liver Biopsy for the Detection of Schistosomiasis Mansoni**
S. G. LATTY, G. W. HUNTER, A. P. MOON, B. H. SULLIVAN, J. C. BURKE, and H. F. SPROAT. *Gastroenterology* [*Gastroenterology*] **27**, 324–333, Sept., 1954. 4 figs., 24 refs.

To determine the most efficient technique for the diagnosis of infection with *Schistosoma mansoni* faeces were examined and rectal biopsy, liver biopsy, and skin tests were carried out on 107 Puerto Rican soldiers who were without symptoms and in whom there was no clinical evidence of schistosomiasis. Three different specimens of stool from each patient were examined by two concentration methods, the hydrochloric-acid–sodium-sulphate–"triton"–ether (AMS III) technique and the formalin–ether (MGL) technique. Rectal biopsy was carried out after the third faecal specimen had been collected, most of the material being taken from the lowermost rectal valve, generally from the anterior wall of the rectum. Liver biopsy was performed in 29 of the cases in which stool examination had proved positive, 6 sections of liver material being examined. For the skin tests a lyophilized antigen preserved with "merthiolate" (thiomersalate) was used. [The paper suggests that the antigen was prepared from cercariae or worms, but the exact source is not stated.]

The results of stool examination were positive in 39 of the 107 cases, and out of 117 specimens, 93 were positive by AMS III and 80 by MGL. The two methods differed little in efficacy, but more eggs were recovered by AMS III than by MGL. In 6 of these 39 positive cases the rectal biopsy specimen was negative, while of 36 cases in which rectal biopsy was positive, 3 were negative by stool examination. Statistically, the diagnostic efficacy of stool examination differed little from that of rectal biopsy. In 14 out of 29 liver biopsy specimens granulomatous lesions were found. Skin tests were carried out on 88 patients, positive reactions being obtained in 49. In 13 of these stool and biopsy examinations proved negative, whereas in 13 known positive cases the reaction to the skin test was negative. No single method of testing revealed the presence of worms in all positive cases.

The authors conclude that the skin test is not reliable, that liver biopsy cannot be recommended as a routine diagnostic procedure, and that in suspected cases 3 stool specimens should be examined (using either AMS III or MGL) and a rectal biopsy performed if eggs are not found.

O. D. Standen

Allergy

1222. **The Effect of Some Sympathicomimetic Amines and Enzyme Blocking Agents on Asthma in the Guinea Pig Induced by Antigen or Histamine Aerosols**
J. REBHUN, S. M. FEINBERG, and E. A. ZELLER. *Journal of Allergy* [*J. Allergy*] **25**, 440–446, Sept., 1954. 8 refs.

Healthy guinea-pigs were exposed to an aerosol of histamine, and guinea-pigs which had previously been sensitized to egg albumen were exposed to an aerosol of egg albumen. In both groups the period of exposure required for the development of severe dyspnoea was determined. This method was utilized at the Northwestern University Medical School, Chicago, for the investigation of the protective action of various substances. Histamine shock was not prevented or delayed by iproniazid or isoniazid, but definite protection was afforded by pyruvic acid *iso*nicotinyl hydrazine. While phenylethylamine had no influence on anaphylactic shock, it protected some of the animals against histamine shock if high doses (30 mg. or more) were given. Amylamine and "tyramine" did not provide protection against histamine shock. Since iproniazid inhibits the adrenaline-destroying enzyme, monoamine oxidase, more adrenaline, it can be assumed, becomes available in the body. In spite of this supposed excess of adrenaline, however, the effect of histamine aerosol remained unchanged. Similarly, the inhibition of the histamine-destroying enzyme, diamine oxidase (histaminase), by isoniazid did not alter the effect of the histamine aerosol. It is concluded that the action of monoamine oxidase cannot be the only factor in the prevention of anaphylactic shock, and that the part played by histaminase in the regulation of histamine shock is negligible. *H. Herxheimer*

1223. **Topical Use of Hydrocortisone Alcohol in the Treatment of Ragweed Hay Fever. Preliminary Report**
H. S. TUFT. *Annals of Allergy* [*Ann. Allergy*] **12**, 687–691, Nov.–Dec., 1954. 12 refs.

A solution containing 0·02% of hydrocortisone alcohol and two different local vasoconstrictors was instilled 3-hourly into the nostrils of 25 patients, mostly young adults, suffering seasonally from ragweed hay-fever. Later on the patients took the treatment only when needed. The measure of the effect of treatment was the duration of the relief of nasal blockage accompanied by less sneezing and rhinorrhoea. If relief lasted from 7 to 10 hours it was considered "excellent" and if from 5 to 7 hours "good". The subjective results of treatment were excellent in 5 cases, good in 8, fair in 6, and poor or absent in 6. In the first two classes the nasal mucosa was found to be less pale and less swollen.

[In this uncontrolled trial three different drugs were used simultaneously; it is therefore difficult to follow the reasons for the author's conclusion that hydrocortisone effectively relieves the rhinitis of hay-fever.] *H. Herxheimer*

1224. **The Serological Examination of Sera from Normal Persons and from Hayfever Patients Both before and after Specific Hyposensitization for Heatstable Antibodies to the Proteins of Timothy Grass Pollen.** [In English]
C. J. C. BRITTON and R. R. A. COOMBS. *Acta allergologica* [*Acta allerg.* (*Kbh.*)] **8**, 31–43, 1955. 8 refs.

In this paper from the University of Cambridge the authors describe the use of two new serological techniques—the "red cell linked antigen test" and the "coated tanned red cell technique"—for the detection of antibodies to pollen in hay-fever patients undergoing specific sensitization. They found that heat-stable antibodies to the antigens of Timothy-grass pollen could be demonstrated in the blood of patients receiving mixed pollen extract. They point out, however, that these tests *in vitro* are likely to be of limited clinical value. *A. W. Frankland*

1225. **Fatal Cases of Allergic Constitutional Reactions. With Some Comments.** [In English]
E. BRUUN. *Acta allergologica* [*Acta allerg.* (*Kbh.*)] **8**, 134–142, 1955. 12 refs.

During a recent 4-year period 5 deaths from specific anti-allergic treatment have occurred in Scandinavia. Four of these cases have already been reported [the references are given], and in the present paper from the University of Copenhagen the author briefly summarizes these and adds details of the fifth case. A man aged 47 with bronchial asthma was desensitized with an extract of purified house dust and then given a maintenance dose of 1 ml. of 1:100 dilution once a week. He tolerated the first 4 maintenance doses, but died within a few minutes of receiving the fifth dose. [No mention is made in the necropsy report of status thymicolymphaticus.] *A. W. Frankland*

1226. **Urticaria and Angioedema. Statistical Survey of Five Hundred Cases**
M. J. STEINHARDT. *Annals of Allergy* [*Ann. Allergy*] **12**, 659–670, Nov.–Dec., 1954. 2 figs., bibliography.

The author reviews 500 cases of urticaria and angioneurotic oedema seen at the University Hospital, Ann Arbor, Michigan, between 1942 and 1953. These disorders were more prevalent during the 2nd and 3rd decades of life and slightly more in females than in males. Skin tests gave little help in the detection of the aetiological factor or factors. Foodstuffs were thought to be the cause in about 30% of the cases, psychological factors in about 25%, drugs in 27%, and infections in 14%. In recent years drugs and psychological factors were more frequently held to be the cause of the disorder than in the earlier years of the period. *H. Herxheimer*

1227. **Intussusception of Vermiform Appendix in Allergic Children**
R. G. MITCHELL. *British Medical Journal* [*Brit. med. J.*] **1**, 265–266, Jan. 29, 1955. 7 refs.

Nutrition and Metabolism

1228. **Fat Emulsions as Caloric Supplements in Parenteral Nutrition, with Particular Reference to Amino Acid Utilization**

P. R. CANNON, L. E. FRAZIER, and R. H. HUGHES. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **44**, 250–260, Aug., 1954. 1 fig., 13 refs.

In experiments carried out at the University of Chicago the effect of parenteral administration of fat emulsions upon the utilization of amino-acids in the synthesis of tissue proteins was studied in a number of rats undergoing protein repletion. The animals were given daily subcutaneous injections of increasing amounts of 10% protein hydrolysate and a 12-Calorie non-protein diet adequate in salts, vitamins, and roughage. The protein hydrolysate injections were standardized at 18 ml. (216 mg. of nitrogen) per rat daily. The animals were then divided into two groups, one group continuing on this regimen and the other receiving fat emulsion stabilized with " tween 60 " either intraperitoneally or intravenously in doses which provided about 20 extra Calories a day. Nutritional performance was assessed from weight gain and from the results of carcass analyses. In the animals receiving protein hydrolysate alone body weight was maintained for 8 days; there then followed a rapid loss of weight, which began when about 70% of the animal's body fat had been utilized. Administion of extra calories in the form of a fat emulsion resulted in rapid conversion of the protein hydrolysate into protein and a progressive gain in weight. The animals receiving fat emulsion gained about 2·5 g. body weight daily, which compared favourably with a gain of 2 g. daily in rats given a 32-Calorie non-protein diet and similar injections of protein hydrolysate. The emulsions were completely utilized, were non-toxic, and did not appear to cause any tissue damage. *A. C. Frazer*

1229. **Will Fat Emulsions Given Intravenously Promote Protein Synthesis? Metabolic Studies on Normal Subjects and Surgical Patients**

T. B. VAN ITALLIE, F. D. MOORE, R. P. GEYER, and F. J. STARE. *Surgery* [*Surgery*] **36**, 720–731, Oct., 1954. 3 figs., 17 refs.

In experiments carried out at Peter Bent Brigham Hospital (Harvard Medical School), Boston, the effect of the intravenous administration of fat emulsions on the metabolism of 2 healthy volunteers and 2 well-nourished patients undergoing subtotal gastrectomy for duodenal ulcer was studied. The fat emulsions used contained 15 g. of vegetable oil, 1 g. of phosphatide, 1 g. of " demal-14 ", and 4·3 g. of dextrose per 100 ml. The first normal subject was given a diet restricting his nitrogen intake to 4 g. a day for 4 days before the experiment. Then for 7 days he received a diet of 947 Calories containing 7·8 g. of nitrogen, 58 mEq. of potassium, and 100 mEq. of sodium daily. During this period the average nitrogen balance was $-3{\cdot}36 \pm 0{\cdot}75$ g. per day and the potassium balance $-14{\cdot}19 \pm 5{\cdot}58$ mEq. per day. He lost an average of 0·26 kg. of body weight per day, and the number of circulating eosinophils decreased. The subject was then given intravenous fat emulsion providing an average of 930 Calories a day for 5 days, the oral intake remaining the same except that the carbohydrate in the diet was reduced to compensate for the calories provided by the dextrose in the emulsion. During this period the nitrogen deficit decreased to $-1{\cdot}16 \pm 1{\cdot}09$ g. per day and potassium balance reached virtual equilibrium at $-2{\cdot}08 \pm 11{\cdot}66$ mEq. per day. There was a weight gain of 0·4 kg. and the circulating eosinophil count rose. When the intravenous fat infusion was discontinued the subject returned to the metabolic state observed before the emulsion was given. The second healthy volunteer was subjected to a more severe restriction of nitrogen intake (3 g. per day), and a similar improvement occurred in the potassium deficit, but not in the negative nitrogen balance, when intravenous fat emulsion was administered.

The two surgical patients were given fat emulsion intravenously during the week immediately following operation, one receiving 1,392 Calories per day and the other 1,270 Calories per day on average, while nitrogen intake was minimal. The administration of the fat emulsion to these patients did not alter the metabolic pattern usually found in this type of case in the immediate postoperative period, but it is emphasized that these observations do not discredit the use of intravenous fat emulsions as a source of extra calories in the later stages of surgical convalescence. *A. C. Frazer*

1230. **Amino-aciduria in Galactosemia**

D. Y. Y. HSIA, H. H. HSIA, S. GREEN, M. KAY, and S. S. GELLIS. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **88**, 458–465, Oct., 1954. 1 fig., 44 refs.

Amino-aciduria was demonstrated when galactose was added to the diet of 2 children with galactosemia. This was confirmed both by quantitative measurements and by paper partition chromatography techniques. The amino-aciduria was generalized and involved several different amino acids. It appeared to be primarily renal and probably toxic in nature. Increased protein catabolism in the body as well as saturation of the renal threshold by galactose might be responsible for the loss of amino acids. It appears unrelated to the action of galactose on the liver. The *alpha* amino nitrogen metabolism of the parents of these children was completely normal.—[Authors' summary.]

1231. **The Action of Chorionic Gonadotrophin in the Obese**

A. T. W. SIMEONS. *Lancet* [*Lancet*] **2**, 946–947, Nov. 6, 1954.

Gastroenterology

1232. **The Fallacy of the Furred Tongue**
B. GANS. *British Medical Journal* [*Brit. med. J.*] **2**, 1146–1147, Nov. 13, 1954. 4 refs.

Having observed during routine infant welfare examinations that many apparently healthy infants had a heavily furred tongue, the author, at Miller Hospital, London, studied the state of the tongue in a series of 750 children aged 2 weeks to 14 years. The children were attending out-patient clinics, and at the time of examination were not suffering from any general illness or any acute local condition of the mouth or throat. No relationship was observed between the presence or absence of fur on the tongue and the state of the tonsils, teeth, or nasal airway. Moreover, no association was established between the state of the tongue and such disorders as enlarged cervical lymph nodes, a poor appetite, and constipation; for example, of 234 children with enlarged cervical lymph nodes, 90 had a clean tongue. It would appear from this investigation that in children of all ages the furred or dirty tongue is without significance.
A. Garland

STOMACH AND DUODENUM

1233. **Magnesium Aluminum Hydroxide Gel in the Antacid Therapy of Peptic Ulcer**
S. MORRISON. *American Journal of Gastroenterology* [*Amer. J. Gastroent.*] **22**, 301–308, Oct., 1954. 15 refs.

The clinical results obtained with magnesium aluminium hydroxide gel in the treatment of 136 cases of peptic ulcer are described in this paper from the University of Maryland School of Medicine, Baltimore. Although the investigation was uncontrolled statistically, the author claims that magnesium aluminium hydroxide gel proved more palatable, less astringent, and less constipating than aluminium hydroxide. He concludes that it is superior to aluminium hydroxide in the antacid therapy of peptic ulcer and hyperchlorhydria.
G. A. Smart

1234. **The Problem of Nutrition following Complete Gastrectomy**
H. J. MCCORKLE and H. A. HARPER. *Annals of Surgery* [*Ann. Surg.*] **140**, 467–474, Oct., 1954. 3 figs., 17 refs.

Studies made following total gastrectomy in 120 dogs with normal and partially gastrectomized animals as controls indicate that in the totally gastrectomized animals: (*a*) Alimentation time is decreased to less than one-half that of the normal controls. (*b*) The rate of absorption of amino acids was more rapid than in the controls, but the efficiency of absorption was reduced as evidenced by increased losses of nitrogen in the stool. (*c*) In most instances, the totally gastrectomized animals remained in positive nitrogen balance. This was achieved, however, only when the gastrectomized animal was able to ingest relatively large quantities of protein. (*d*) The absorption of glucose was accelerated after gastrectomy, but there was also a more rapid fall in the blood sugar levels. (*e*) The rate of absorption of fat was moderately increased, although not to the same extent as amino acids or glucose. (*f*) Anemia occurs following total gastrectomy, but may be minimized by supplementary vitamin therapy. (*g*) In dogs following total gastrectomy, good nutrition and weight were maintained if the animals could be given isoperistaltic continuity between the esophagus and duodenum and if they could be trained to eat slowly.

In human patients following total gastrectomy: (*a*) it also appears to be preferable to maintain continuity between the esophagus and duodenum. This can be done by esophagoduodenostomy, or by anastomosing an isoperistaltic segment of jejunum or colon between the distal esophagus and proximal duodenum; and (*b*) apparently, in spite of decreased alimentation time and some alterations in carbohydrate, protein and fat utilization and a tendency to anemia, it is possible to maintain weight and normal activity, if appetite and capacity for food and digestive comfort can be achieved. This was accomplished in 3 patients in whom isoperistaltic segments of colon were anastomosed to the duodenum and esophagus. This method of restoration of gastrointestinal continuity following total gastrectomy is difficult to achieve technically, but it appears to be worth further trial.—[Authors' summary.]

1235. **Combined Vagus Resection and Partial Gastrectomy for Duodenal and Marginal Ulcer**
L. T. PALUMBO, T. T. MAZUR, and B. J. DOYLE. *Archives of Surgery* [*Arch. Surg. (Chicago)*] **69**, 762–768, Dec., 1954. 10 refs.

The authors report, from the Veterans Administration Hospital, Des Moines, Iowa, the results in 6 out of 42 patients (average age 42) suffering from duodenal and anastomotic ulcers who were treated by partial (75%) gastrectomy with the addition of subphrenic vagectomy, a section of both vagus nerves being excised below the diaphragm. An antecolic anastomosis with a short afferent loop was performed. This operative technique was introduced in 1947 and it was hoped that by the combined procedure, with its consequent reduction of acid secretion in the gastric remnant, the incidence of anastomotic ulcer would be diminished; that by reason of the reduction in gastric motility the incidence of the dumping syndrome would be reduced; and that if both these expectations were realized it might be possible in future cases to perform a more limited gastrectomy, thus offering the advantages of a larger gastric pouch.

That these hopes were not wholly fulfilled is shown by the results, which were as follows. Of 36 patients

followed up for an average period of 43 months (maximum, 78 months), one died from peritonitis following perforation of the duodenal stump. Of the remaining 35, 14 (42%) gained weight but an equal number lost weight, 22 (63%) were able to return to a normal diet and three meals a day (the remaining 13 requiring a restricted diet and more frequent meals), 22 (63%) had a good capacity for work, 4 (11%) a fair capacity, 3 (8·5%) poor capacity, and 6 (17·5%) were unable to work. Persistent diarrhoea occurred in 9 cases (21%), the dumping syndrome in 7 (although it was mild in 3 cases), gastric discomfort after too large a meal in 6 cases, and ulcer-like pain in one; 28 (80%) of the patients were free from pain. The Hollander insulin test showed the absence of acid in all patients even up to 6½ years, this achlorhydria suggesting that there was no regeneration of the vagus pathways. On the credit side is the fact that no anastomotic ulcers have occurred during the period of observation. On the whole, however, the results are considered disappointing, particularly in regard to the incidence of the dumping syndrome, which was little lower than after simple gastrectomy. The authors consider that the results do not justify the general adoption of vagus resection as an accompaniment to ordinary gastrectomy, but believe that the combined operation has a place in the treatment of patients with evidence of an unstable autonomic nervous system in whom the psychogenic secretion of gastric juice is excessive. *Charles P. Nicholas*

1236. **Partial Gastrectomy: Ten Years Later**
C. Wells and I. W. MacPhee. *British Medical Journal* [*Brit. med. J.*] **2**, 1128–1132, Nov. 13, 1954. 1 fig., 11 refs.

In a series of 119 patients treated for peptic ulcer by partial gastrectomy 10 or more years ago, 75 patients have been regularly examined and their progress studied. The following conclusions were drawn.

With any type of anastomosis, the incidence of recurrent ulcer varies inversely with the extent of the gastric resection. With the Polya type of anastomosis, the incidence of bilious vomiting and associated symptoms varies directly with the extent of the gastric resection. Serious post-gastrectomy symptoms may not develop until many years after the operation. If direct gastro-duodenal continuity is not re-established at the time of operation, hypochromic anaemia is apt to occur. A more limited gastric resection combined with vagotomy and a gastro-duodenal anastomosis may represent the Aristotelian mean in the surgery of peptic ulcer.—[Authors' summary.]

1237. **Colonic Symptoms with Active Duodenal Ulcer**
S. P. Seigle and B. V. White. *New England Journal of Medicine* [*New Engl. J. Med.*] **251**, 693–694, Oct. 21, 1954. 7 refs.

Recurrent symptoms of an irritable colon are sometimes the principal or only clinical evidence of active duodenal ulcer, such symptoms including constipation, alternating constipation and diarrhoea, hard stools with mucous, excessive gas in the bowel, and colonic pain. The incidence of these symptoms in a series of 269 cases of duodenal ulcer analysed at the Hartford Hospital, Hartford, Connecticut, was 40%. The colonic symptoms occurred at the same time as the ulcer discomfort and activity; only in a minority of the patients (4·5%) did they appear to be an independent phenomenon. It is pointed out that the manifestations of an irritable colon may overshadow the symptoms of duodenal ulcer and so lead to errors in diagnosis. *J. Naish*

1238. **Electrolyte Depletion in Pyloric Stenosis**
D. A. K. Black and R. P. Jepson. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **23**, 367–382, Oct., 1954. 4 figs., 24 refs.

From Manchester University Medical School the authors report the results of electrolyte balance studies carried out on 7 patients with pyloric stenosis and 4 with peptic ulceration but no pyloric stenosis. The intake and urinary output of sodium, chloride, and potassium were measured from the day the patients came under observation until one week after the performance of partial gastrectomy; serum levels of sodium, potassium, chloride, and bicarbonate were also estimated at intervals.

The serum sodium concentration was significantly low in only one patient with pyloric stenosis, and serum potassium concentration was also within the normal range in all cases. In the 7 cases of pyloric stenosis serum bicarbonate levels were high, and in 2 of these serum chloride concentration was abnormally low. At one week after operation there was little change in the serum levels of sodium or potassium, but in the patients with stenosis the serum bicarbonate level decreased, the chloride concentration increasing to a corresponding extent.

It was apparent from the balance studies that 2 of the patients with pyloric stenosis had well-marked sodium depletion. The others retained much the same amount of sodium after operation as did the patients without stenosis. Of the 5 patients who had shown clinical signs of pyloric stenosis preoperatively, one had a marked and 3 a moderate degree of potassium depletion, and one, having received large amounts of saline, probably had not attained potassium equilibrium at the end of the period of study. All the patients retained chloride after operation, this being small in amount (168 mEq.) in the case of those without stenosis and in the 2 cases of partial stenosis found at operation. The 5 patients with clinical signs of pyloric stenosis, however, retained large amounts of chloride (279 to 1,890 mEq.). When these positive balances were considered in conjunction with the changes in serum chloride level it was obvious that the extracellular fluid volume, although increased in some cases, could not have expanded to the extent necessary to retain these amounts (assuming that chloride remains in the extracellular fluid compartment). It seemed most probable, then, that some chloride must have gone into the intracellular compartment.

When the electrolyte balance was considered as a whole there seemed to be little correlation between the degree of sodium and potassium depletion, suggesting that the mechanism of depletion is different for each of

the two elements. Patients without pyloric stenosis retained more chloride than sodium plus potassium; but those with clinical pyloric stenosis all retained much more sodium plus potassium than chloride, in spite of which the serum alkali reserve in these cases fell and chloride concentration increased. The most likely explanation would seem to be that there was an intracellular acidosis associated with potassium loss, and an extracellular alkalosis. It is suggested, therefore, that patients who are severely dehydrated should be treated with sodium chloride solution intravenously and potassium by mouth in the form of an alkaline potassium mixture. When not clinically dehydrated they should not be given intravenous saline, but potassium salts (about 100 mEq. of potassium per day) should be given by mouth until they can take a normal diet. Ammonium chloride should play no part in the treatment of pyloric stenosis. *G. A. Smart*

LIVER

1239. **Dietary Protein in the Genesis of Hepatic Coma**
R. SCHWARTZ, G. B. PHILLIPS, J. E. SEEGMILLER, G. J. GABUZDA, and C. S. DAVIDSON. *New England Journal of Medicine* [*New Engl. J. Med.*] **251**, 685–689, Oct. 21, 1954. 3 figs., 15 refs.

From Boston City Hospital 3 cases of cirrhosis of the liver are described in which there was intolerance to administration of dietary protein. In one case the daily intake of protein was twice raised from 50 to 75 g., and on each occasion this increase was followed by mental confusion, tremor, and specific changes in the electroencephalogram. In 2 cases which were fatal a high serum ammonia level and a low serum sodium level were associated with hepatic coma.

The authors conclude that whatever the exact mechanism of hepatic coma may be, protein intake is the critical factor, and that signs of tremor should be looked for and the electroencephalogram and serum ammonia level closely studied before making any increase in the protein intake of a patient with cirrhosis of the liver. They believe that individual tolerance for protein depends on the stage and severity of the disease.

J. Naish

1240. **Blood Ammonia, Experimental and Clinical Study in Abnormalities of the Liver and Portal Circulation**
J. D. MANN, J. L. BOLLMAN, K. A. HUIZENGA, T. FARRAR, and J. H. GRINDLAY. *Gastroenterology* [*Gastroenterology*] **27**, 399–410, Oct., 1954. 5 figs., 23 refs.

The relative importance of liver damage and derangement of the portal circulation in determining abnormalities of ammonia metabolism was studied by the authors at the Mayo Clinic in patients with various diseases of the liver and other organs and in experiments on dogs. In agreement with other workers, they found that the blood ammonia level was often above normal in patients with hepatic cirrhosis, the highest levels of all being found in 4 of 5 patients in hepatic coma. In dogs the blood ammonia content was increased by by-passing the liver by means of an Eck fistula or by progressive obstruction of the portal vein, although there was no rise in the level in dogs exposed to repeated doses of carbon tetrachloride [on which, however, no biochemical tests of liver function were carried out]. Variations in diet and the administration of antibiotics had little effect on the blood ammonia level, but in dogs with an Eck fistula the level was low after fasting and rose after a meat meal.

Ammonia was given to dogs by intravenous infusion at various rates, and although under these conditions high levels of blood ammonia were obtained in the animals with Eck fistula, coma was not observed. Cannulation of the hepatic and pulmonary veins showed that the liver removed ammonia at about the same rate in dogs with an Eck fistula or ligated portal vein as in normal dogs, although there was a reduced hepatic ammonia clearance, attributable to by-passing of the liver and reduced hepatic blood flow, so that to obtain this presumably maximal rate of removal of ammonia a higher concentration in arterial blood was required.

P. C. Reynell

1241. **Methyl Mercaptan in Relation to Foetor Hepaticus**
F. CHALLENGER and J. M. WALSHE. *Biochemical Journal* [*Biochem. J.*] **59**, 372–375, 1955. 26 refs.

A case of massive hepatic necrosis exhibited foetor hepaticus in the breath and a similar odour in the urine. Passage of nitrogen through the urine into mercuric cyanide yielded mercury dimethyl mercaptide $Hg(SCH_3)_2$. The probable source of the methyl mercaptan is the CH_3S– group of methionine, the normal demethylating processes being inhibited by liver damage. Both methyl mercaptan and dimethyl disulphide may be exhaled in the breath. Analogous reactions in certain micro-organisms, and with the enzyme thionase, and the toxicity of methionine to man and animals are considered.—[Authors' summary.]

1242. **Acute Hepatic Insufficiency of the Chronic Alcoholic. Clinical and Pathological Study**
G. B. PHILLIPS and C. S. DAVIDSON. *Archives of Internal Medicine* [*Arch. intern. Med.*] **94**, 585–603, Oct., 1954. 8 figs. 37 refs.

A detailed account is given of the clinical and pathological findings in 56 patients admitted to the Boston City Hospital with chronic alcoholism, in all of whom hepatic insufficiency was present, with particular reference to the presence and significance of a type of hepatic damage to which, according to the authors, attention was first drawn by Mallory in 1911 (*Bull. Johns Hopk. Hosp.*, 1911, **22**, 69). This lesion is additional to the invariable fibrosis and frequent fatty change in cirrhosis and is characterized by " hyaline degeneration and necrosis of parenchymal cells with leucocytic infiltration ", and the authors' main purpose was to discover whether its presence in chronic alcoholic cirrhosis has any marked effect on the prognosis of the case.

Of their 56 cases, 2 were excluded because the findings were indefinite. In 28 cases the presence of the Mallory lesion in severe degree was demonstrated either post mortem or by liver biopsy, and 18 of these patients died

in hospital, generally in coma. In the remaining 26 cases, in which liver biopsy failed to show the lesion in severe degree, mortality was much lower, only 4 of them ending fatally in the wards. Fibrosis of the liver was present in all the fatal cases, but fatty changes were very variable and sometimes practically absent. Various photomicrographs illustrating the characteristic appearances in the liver are reproduced. An interesting clinical point is that in patients in whom the Mallory lesion was demonstrable there was generally a well-marked and progressive polymorphonuclear leucocytosis.

The authors conclude that the presence or absence of the lesion described by Mallory is of the greatest importance in the prognosis of hepatic insufficiency in chronic alcoholism.

[This is an important article, but it is regrettable that all but one of the numerous references are to American publications.] *J. W. McNee*

INTESTINES

1243. **A Form of Acute Hemorrhagic Enterocolitis Afflicting Chronically Ill Individuals. A Description of Twenty Cases**

R. WILSON and R. E. QUALHEIM. *Gastroenterology* [*Gastroenterology*] **27**, 431–444, Oct., 1954. 4 figs., 36 refs.

The authors describe in tabular form the clinical and pathological features of 20 fatal cases of acute haemorrhagic enterocolitis occurring between 1947 and 1953 at the Cincinnati General Hospital (University of Cincinnati), 8 having been observed by the authors during the last 1½ years and the remaining 12 having been collected from the hospital records. The incidence among necropsies on adults over 30 years of age was 0·6%.

The majority of these patients were elderly, only 4 being under 60 years of age, and 17 had chronic cardiovascular disease, 13 of these being in congestive failure on admission. In 2 cases (both in females of 72) the enterocolitis followed an operation (for fracture of the neck of the femur and for strangulated ileum respectively), and in one case (in a man of 73) its onset was preceded by a small cerebral thrombosis.

Onset was sudden, with acute cramping or aching abdominal pain, either generalized or localized to the epigastrium and umbilical region. Diarrhoea was usual and occasionally bloody, while shock was either present on admission or noted soon after. In only one case was the correct diagnosis made on clinical grounds, the most common clinical diagnosis made being acute mesenteric thrombosis, which led to operative intervention in 2 cases. In 8 cases intra-abdominal disease was not suspected. Treatment was supportive and included the administration of antibiotics, but the disease ended fatally in 1 to 5 days.

At necropsy large amounts of blood were found in the intestinal lumen even though blood had not been present in the stools. The length of gut affected varied, the entire length of the small and large intestines being involved in some cases, while in others the lesions were confined to parts of the colon or the stomach and duodenum. The serosa was injected, but peritonitis was absent, except in 2 cases where foci of peritonitis overlay deep intestinal ulcerations. The submucosa was oedematous and there were varying degrees of haemorrhage in the mucosa and, in advanced cases, the submucosa. No haemorrhage was found in the muscularis. The mesenteric vessels were patent and no evidence was found of necrotizing angiitis or severe arteriolar sclerosis. Various pathogens were isolated from different parts of the gut, but were considered to be secondary invaders.

Speculating on the aetiology of the condition, the authors suggest, admittedly without proof, that "intestinal capillary breakdown initiates the process and . . . that senility, malnutrition, and congestion and anoxia of the intestinal capillaries secondary to heart failure . . . are in part responsible for weakening of the vessel walls. In this situation, fluid, protein, and finally red cells leak into the surrounding tissue. Edema, necrosis, ulceration, additional hemorrhage, secondary infection, shock, and death of the whole organism ensue". One illustrative case is described in detail. *H. F. Reichenfeld*

1244. **Erythema Nodosum in Ulcerative Colitis**

J. J. FOSTER and I. B. BRICK. *Gastroenterology* [*Gastroenterology*] **27**, 417–425, Oct., 1954. 16 refs.

After reviewing references in the literature to erythema nodosum occurring in the course of ulcerative colitis the authors describe in detail 3 such cases seen at Georgetown University Hospital, Washington, D.C. All 3 patients were female, they were between 41 and 52 years of age, and the colitis was of some 2 to 6 years' standing, the diagnosis having been established radiologically and by sigmoidoscopy. In each case, during an acute exacerbation manifested by increase in diarrhoea, fever, and loss of weight, the patient developed lesions on the legs which in 2 cases were definitely diagnosed as erythema nodosum, while in the third case the same diagnosis seemed likely from the patient's description of the lesions. Simultaneously these patients suffered from non-purulent conjunctivitis or blepharitis and arthralgia affecting one or more of the joints of the extremities. All 3 patients were treated with corticotrophin (ACTH), 5 to 20 mg. daily being administered by intravenous drip infusion in 5% dextrose solution for 4 to 5 days, the dose being gradually reduced and the treatment finally stopped entirely or replaced by a short course of cortisone by mouth. With this treatment there was symptomatic improvement, with disappearance of the skin lesions and arthralgia, but subsequent exacerbations of the colitis were again accompanied by the appearance of erythematous nodules.

Four further cases are cited from the records of the same hospital, 3 of these being in females between 23 and 31 and the fourth in a 33-year-old male. The appearance of the skin lesions coincided in each case with a period of activity of the colitis, and other known causes of erythema nodosum were excluded. These 7 cases occurred among a total of 37 patients with ulcerative colitis treated between August, 1947, and August, 1953. *H. F. Reichenfeld*

Cardiovascular System

CONGENITAL HEART DISEASE

1245. **The Presence of Venoarterial Shunts in Patients with Interatrial Communications**
H. J. C. Swan, H. B. Burchell, and E. H. Wood. *Circulation* [*Circulation (N.Y.)*] **10**, 705–713, Nov., 1954. 3 figs., 24 refs.

In patients with uncomplicated atrial septal defect there is normally a left-to right (arteriovenous) shunt, but reversal of this shunt may occur in association with heart failure, pulmonary hypertension, or pulmonary stenosis. However, it is possible that small right-to-left (venoarterial) shunts may not be detected by measurement of the arterial oxygen saturation, because of the wide variation in normal values. Working at the Mayo Clinic, University of Minnesota, the authors have used a more sensitive technique in which azovan (Evans) blue (T-1824) is injected through a cardiac catheter and the dilution curves recorded by means of an ear oximeter. The pattern of the curve will demonstrate the presence of a shunt.

In the clinical application of this method the injection of dye into the inferior vena cava produced evidence of small right-to-left shunts in 9 out of 11 patients with atrial septal defect. In contrast, only 4 patients showed venoarterial shunts when the dye was injected into the superior vena cava. This finding is explained by the fact that the limbus of the fossa ovalis straddles the orifice of the inferior vena cava, whereas the opening of the superior vena cava is directed towards the tricuspid valve. From this the authors argue that it should be possible to predict the approximate site of the septal defect by analysing the pattern of the dilution curves from the venae cavae. Such a prediction was made in 5 cases in 4 of which it was confirmed at operation.

A. Paton

1246. **Modes of Healing following Surgical Closure of Experimental Atrial Septal Defects**
A. A. Pomeranz, E. Watkins, and R. E. Gross. *Archives of Surgery* [*Arch. Surg. (Chicago)*] **69**, 870–885, Dec., 1954. 9 figs., 19 refs.

The necessity for study of many methods of repairing septal defects stems from the variability of interatrial septal orifices which occurs in man. These variations in size, shape, and location in the septum indicate that it is desirable to have at hand several different methods for closure of defects as they are approached in humans.

A comparative study has been made of the serial healing patterns in the dog heart following immediate closure of defects which were created in the atrial septum. Methods of closure subjected to study were: (1) repair by means of rigid plastic screw-on buttons; (2) suture coaptation of the defect edges; (3) use of autologous free grafts of pericardium or vein, or use of free grafts of autologous or homologous atrial appendage; (4) closure by suture onlay of rigid plastic discs or of onlay of pliable nylon or polyethylene sheet to cover the defect.

All of the methods of repair in the experimental animal led to a rather uniform pattern of healing by thrombus formation over the region of the closure and by endothelization of the surface of the thrombus. Thrombi were gradually transformed into fibrous scars. Autologous and homologous free-tissue grafts were replaced with fibrous tissue. The foreign materials studied were accepted by the heart in an amazing manner and became an integral part of the septum.

A number of considerations have led us to the conclusion that auricular defects in the human can be closed by simple suture coaptation of smaller openings, whereas very large openings can be repaired well by the onlay of a sheet of plastic material, for which polyethylene film, 0·5 mm. thick, has suitable properties.—[Authors' summary.]

1247. **The Tetralogy of Fallot in the Adult.** (La tetrade di Fallot nell'età adulta)
P. F. Angelino, A. Actis-Dato, and V. Levi. *Cardiologia Pratica* [*Cardiol. prat.*] **5**, 329–351, Aug., 1954. 4 figs., 16 refs.

About one-fifth of all patients with Fallot's tetralogy reach adult life, and among these females predominate. The authors have studied 13 patients ranging in age from 20 to 32 at the Surgical Clinic of the University of Turin. Physical development was normal, though physical activity was reduced in all except one case. Cyanosis and clubbing of the fingers were present in the majority, and dorsal scoliosis was a marked feature in 8 cases. Episodes of haemoptysis had occurred in 6 cases, and were thought to be due to the presence of an extensive collateral circulation, which gave the lungs a "plethoric" appearance on radiography in contrast to the "anaemic" appearance of the lungs of infants with this disease. It is considered probable that prolongation of life is due to the development of this collateral circulation rather than to minor degrees of pulmonary stenosis and dextroposition of the aorta, as has been thought in the past. Endocarditis occurred in only one patient, and pulmonary tuberculosis was not observed. All the patients had albuminuria, but renal function was normal. Electrocardiography, angiocardiography, and cardiac catheterization produced results similar to those found in children.

The risks of operation in this condition increase with age because of the fragility of the pulmonary artery and the extent of the collateral circulation, and of the 9 patients who were subjected to operation, 3 died. Blalock's operation is nearly always technically impossible, and could be carried out in only one of these

patients. The operation of choice is probably Pott's method of aorto-pulmonary anastomosis, which was carried out on 6 patients. Pulmonary valvotomy was performed on one subject with excellent results, while thoracotomy only was undertaken in another. The post-operative course was always prolonged. *A. Paton*

PERICARDIUM

1248. **Surgical Treatment of Chronic Constrictive Pericarditis**

H. B. SHUMACKER. *American Surgeon* [*Amer. Surg.*] **20**, 1137–1149, Nov., 1954. 15 refs.

In this discussion of the surgical treatment of constrictive pericarditis the author, drawing on his own experience at Indiana University School of Medicine, Indianapolis, and on that reported in the literature, attempts to answer the important questions: (1) at what stage should operation be done; (2) in cases of tuberculous pericarditis should a reduction in the activity of the tuberculous process be awaited before operation is carried out; (3) over which chambers of the heart is decompression most essential; (4) what is the most satisfactory approach to the heart; and (5) what are the causes of an imperfect result of pericardectomy?

Of 9 personal cases reported in detail, 7 were of typical chronic constrictive pericarditis; in 5 of these the patient was returned to normal health by operation. There was one death, that of a man whose operation had been deferred in the hope that the activity of the tuberculous process would die out; this, however, did not occur, and pericardectomy was performed with the patient *in extremis*.

The author concludes that operation should be considered as soon as the diagnosis is made and carried out as soon as possible after a short period of treatment by rest, administration of diuretics, and sodium restriction; that activity of tuberculous disease is not a contra-indication to early operation; that decortication should be extensive and, if possible, should include the atria and the great vessels, as well as both ventricles; and that a failure to relieve symptoms in the absence of associated valvular disease is usually due to inadequate decortication. The various surgical approaches which have been employed are discussed; of these the author prefers complete splitting of the sternum with wide retraction of the divided edges, which gives good exposure.

A. M. Macarthur

1249. **Tuberculous Pericarditis in the Adult. (Value of Systematic Electrocardiography.)** (La péricardite tuberculeuse de l'adulte. (Intérêt de l'électrocardiographie systématique))

E. BENHAMOU, E. ALBOU, and J. LAABAN. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur*] **47**, 785–794, Oct., 1954. 11 figs., 16 refs.

The authors believe that pericarditis is a more frequent complication of tuberculosis in adults than is realized, and therefore that more frequent electrocardiographic examinations should be made in cases of pulmonary tuberculosis. Three case histories are described; in 2 purulent tuberculous pericarditis occurred as a complication of miliary tuberculosis and serofibrinous pleuroperitonitis respectively, and in the third a serofibrinous pericarditis complicated tuberculous pleurisy. Illustrative radiographs and electrocardiograms (ECGs) are reproduced.

Although tuberculous pericarditis generally presents with gross clinical signs, it may in some cases be " silent " and in others may present relatively normal *x*-ray appearances, particularly when the pericarditis is concurrent with other tuberculous lesions. In such cases the diagnosis can often be made by electrocardiography. Characteristic changes in the ECG include depression of the ST segment, which assumes a shape like an inverted watch glass and thus can be distinguished from the depressed ST of coronary thrombosis. There may also be inverted T waves and low-voltage curves. The cardiac silhouette may be little or greatly enlarged, or be " mitral-shaped ", but is always relatively immobile on screening.

Diagnosis must be confirmed by withdrawal of pericardial fluid for smear examination, culture, and guinea-pig inoculation. After the injection of air into the pericardial cavity, a fluid level and thickened parietal pericardium can be demonstrated radiologically. Electrophoresis shows a high gamma-globulin content in the effusion and a high α_2-globulin level in the serum, thus distinguishing the condition from acute infective pericarditis in which the gamma-globulin content is high in both the effusion and the serum. The authors recommend treatment with streptomycin and isoniazid given locally as well as parenterally, especially if the pericardium is much thickened, since estimation of the isoniazid level in the pericardial effusion shows that parenteral administration alone of this drug is inadequate, the maximum concentration attained being 2 to 4 μg. per ml. in their cases. *D. Goldman*

1250. **Acute Pericarditis due to Infection with a Known Organism.** (Les péricardites infectieuses aiguës à germe connu)

E. BENHAMOU, E. ALBOU, and J. LAABAN. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur*] **47**, 795–806, Oct., 1954. 16 figs., 15 refs.

The authors describe 6 cases of acute infective pericarditis, with details of the clinical course, *x*-ray appearances, and electrocardiographic (ECG) findings. The first 2 were cases of purulent pneumococcal pericarditis, one of which was associated with massive lobar pneumonia and was cured by local and parenteral administration of penicillin, the other being successfully treated by local and parenteral administration of penicillin and streptomycin. The 3rd case, one of purulent staphylococcal pericarditis following a furuncle, was not relieved by medical treatment, but was cured by pericardiotomy. The 4th, a case of staphylococcal septicaemia with pericarditis and meningitis, was arrested with erythromycin and cleared up with penicillin and streptomycin. The 5th case was of long-standing, purulent, staphylococcal pericarditis complicated by pleurisy, and did not respond to antibiotics. The last case was one

of sero-sanguineous pericarditis presenting during the course of meningococcal meningitis; in this case no organism was isolated, but a good response was obtained to penicillin and streptomycin.

In diagnosis constant physical signs in all cases were: (1) precordial pain, (2) persistent paroxysmal cough not explained by lung disease, (3) greatest relief from lying on the left side. Dyspnoea was not constant, but in all cases the jugular veins were distended and the liver enlarged. The ECG record was found to change progressively with the disease; at first the ST segment was elevated, but later it assumed an inverted watch-glass appearance, while the T wave became flattened or negative; then, in the stage of early recovery, the ST displacement lessened, the T wave remaining negative, until finally there was a return to normal or the ST change remained with a negative T wave. By means of pneumoradiography of the pericardium pericardial fluid can be differentiated from pleuritic effusion and pericardial thickness estimated. A quantity of fluid should be aspirated for the estimation of purulence, for electrophoretic examination, and for culture. The authors recommend early treatment with antibiotics given both locally and parenterally. Because of rapid accumulation of fluid pneumococcal pericarditis usually requires surgical intervention. In some cases streptokinase and hyaluronidase were also injected into the pericardial cavity.

D. Goldman

CORONARY DISEASE AND MYOCARDIAL INFARCTION

1251. **The Relation of Physical Activity and Occupation to Coronary Artery Heart Disease**
J. G. BENTON and H. A. RUSK. *Annals of Internal Medicine* [*Ann. intern: Med.*] **41**, 910–917, Nov., 1954. 3 figs., 20 refs.

This is a review of the available literature in English on the relation of physical activity and occupation to coronary disease, no new data being provided. The conclusion is reached that death from coronary disease is associated with sedentary rather than active occupations and that with proper selection of cases physical activity is not contraindicated in the rehabilitation of patients suffering from this condition.

C. Bruce Perry

1252. **Lipoproteins, Aging, and Coronary Artery Disease**
A. R. TAMPLIN, B. STRISOWER, O. F. DELALLA, J. W. GOFMAN, and F. W. GLAZIER. *Journal of Gerontology* [*J. Geront.*] **9**, 404–411, Oct., 1954. 2 figs., 8 refs.

The authors, working at the University of California, have previously reported (*Science*, 1950, **111**, 166 and 186; *Abstracts of World Medicine*, 1950, **8**, 247) the separation of serum lipoproteins into a number of groups based on their flotation rates in a strong centrifugal field, these being expressed in Svedberg units (S_f). In the present paper the distribution of two main groups of these lipoproteins, designated as S_f 0-12 and S_f 12-400, is considered in relation to coronary arterial disease. For this purpose the disease is regarded as being a chronic accumulative process, and the authors suggest that examination of the coronary arteries in living subjects would reveal a continual gradation in the severity of the disease, independent of whether or not clinical manifestations are present, roughly proportional to age but more directly proportional to the "effective" concentrations of the serum lipoproteins. From a study of two comparable groups of men, one with and one without overt coronary arterial disease, they concluded that the serum concentration of S_f 12-400 lipoproteins is 1·6 times as important as the serum concentration of S_f 0·12 lipoproteins in segregating subjects with coronary disease. From this basis they calculate that the amount of "accumulated coronary artery disease" in any individual is represented by the sum of the values for serum concentration of the two classes of lipoproteins in the ratio of 1:1·6, each being multiplied by the length of time this value has been present. [For details of the mathematical methods employed the original paper should be consulted.]

The theory was tested by applying the formula to calculate the expected mortality from coronary disease in relation to age and sex and comparing the result with the observed mortality as reported in tables of vital statistics. It is claimed that good agreement was obtained. The formula was also used to assess the prognosis in coronary arterial disease over a 10-year period beyond the date on which the serum concentration of lipoprotein fractions was determined.

M. J. H. Smith

1253. **Clinical and Experimental Studies in the Treatment of Coronary Artery Insufficiency by Internal Mammary Artery Implant**
A. VINEBERG. *Journal of the International College of Surgeons* [*J. int. Coll. Surg.*] **22**, 503–518, Nov., 1954. 6 figs., 9 refs.

The author considers that the value of any new surgical procedure should be firmly established in the laboratory before that procedure is used in the treatment of human disease. To this end he has carried out experiments at McGill University, Montreal, on dogs to ascertain the value of implantation of the internal mammary artery in the treatment of coronary arterial disease. After discussing the anatomy of the blood supply of the heart and the pathology of coronary atheroma, he briefly describes the technique of the operation, in which the internal mammary artery is sewn into a tunnel in the myocardium but the sixth intercostal branch is not ligated. From these experiments he established: (1) that an anastomosis develops and stays patent for long periods; (2) that the blood flows towards the heart; and (3) that the implant gives protection to the experimental animals against artificially produced gradual coronary occlusion.

This operation was performed on 12 patients, most of whom had angina on exercise, a few had angina at rest, and several had already suffered infarction. The author points out that the operation will be of no avail unless there is a reasonable amount of viable myocardium to

be revascularized. Contraindications are ventricular failure, advanced essential hypertension, recent myocardial infarction, and left ventricular enlargement. Of the 12 patients, 3 died, 8 were considerably improved, and one did not benefit from the operation.

J. R. Belcher

1254. **Revascularization of the Heart by Anastomosis between Aorta and Coronary Sinus. The Beck II Operation—an Experimental Study**

D. S. LEIGHNINGER and J. DALEM. *Annals of Surgery* [*Ann. Surg.*] **140**, 668–674, Nov., 1954. 4 figs., 13 refs.

Experiments were performed at the Western Reserve University School of Medicine, Cleveland, Ohio, in order to determine more precisely the degree of protection against coronary occlusion afforded by the Beck II operation (arterialization of the coronary sinus by means of a venous graft between the aorta and the sinus) in dogs. The effect of ligation of the circumflex branch of the left coronary artery was studied in: (1) normal dogs; (2) dogs subjected to the Beck II operation 6 weeks previously; and (3) dogs similar to those in Group 2 but in which simultaneous ligation of the graft between the aorta and coronary sinus was carried out. The results were judged on the basis of the mortality in each group and the average size of infarct in surviving animals.

This provided a more searching test than that originally applied by Beck, which consisted essentially in a comparison between Groups 1 and 2 only. Of the 20 dogs in Group 1, 18 (90%) died; of the 20 in Group 2, 9 (45%) died; and of the 15 in Group 3, 8 (53·3%) died. In the 2 surviving animals of Group 1 were found 4 large and one medium-sized infarcts; of the 11 survivors in Group 2, 4 had no infarcts, and in the remaining 7 one medium-sized, 3 small, and 4 very small infarcts were found. In the 7 survivors of Group 3 one large, 3 medium-sized, 2 small, and 2 very small infarcts were found, the heart of one animal containing no infarcts while that of another was not examined. Early death was caused by ventricular fibrillation, while late death was due to heart failure.

It has been shown that the Beck II operation provides additional blood supply to the myocardium by two mechanisms, the first being a retrograde flow from the graft through the capillary bed, which is transient and lasts for about 6 weeks, and the second being by the development of permanent intercoronary arterial channels as a result of the operation.

The authors conclude that the clinical application of this operation in cases of coronary disease should be considered.

C. A. Jackson

1255. **Use of Intestinal Loops for Revascularization of the Heart**

I. D. BARONOFSKY, J. L. SPRAFKA, and J. F. NOBLE. *Circulation Research* [*Circulat. Res.*] **2**, 506–508, Nov., 1954. 1 fig., 9 refs.

In a series of dogs Roux-en-Y loops of small intestine were brought through the diaphragm and sutured to the heart after the serosa of the gut and the epicardium of the heart had been stripped from these structures. Arterial vascular channels could easily be demonstrated between these organs by injection technics and histologic study. The vascular channels formed were large enough to allow passage of thick barium sulfate suspensions.—[Authors' summary.]

1256. **Myocardial Rupture and Hemopericardium Associated with Anticoagulant Therapy. A Post-mortem Study**

B. R. WALDRON, R. H. FENNELL, B. CASTLEMAN, and E. F. BLAND. *New England Journal of Medicine* [*New Engl. J. Med.*] **251**, 892–894, Nov. 25, 1954. 11 refs.

The authors have attempted to ascertain the effect of anticoagulants on the incidence of haemopericardium in patients dying of acute myocardial infarction. An examination of the records of the necropsies carried out at the Massachusetts General Hospital, Boston, between 1932 and 1951 revealed 545 cases in which there had been recent myocardial infarction, in 79 of which there was associated haemopericardium. These 79 cases were divided into two groups: those occurring before 1945, when anticoagulants were not used (Period 1), and those occurring after that date, when anticoagulants were used (Period 2), the latter group being divided into cases in which anticoagulants were given and those in which they were not.

The authors' observations indicated that the incidence of haemopericardium with or without myocardial rupture was not significantly different during Periods 1 and 2 in those patients who did not receive anticoagulants. However, there was a threefold rise in the incidence of haemopericardium without rupture and a twofold increase in the incidence of myocardial rupture among patients who received anticoagulants during Period 2. The frequency of haemopericardium increased with the anticoagulant effect, but, as the authors point out, the groups were too small for the differences to be statistically significant. The administration of anticoagulants did not appear to influence the time of rupture of the myocardium.

E. G. Rees

1257. **The Selective Use of Anticoagulants in Acute Myocardial Infarction Based on Initial Prognosis**

M. M. HALPERN, L. LEMBERG, M. BELLE, and H. EICHERT. *Annals of Internal Medicine* [*Ann. intern. Med.*] **41**, 942–951, Nov., 1954. 22 refs.

An attempt was made in 167 cases of acute myocardial infarction studied at the Jackson Memorial and Mercy Hospitals, Miami, Florida, to assess the prognosis on admission and again after 24 and 48 hours as a guide to the use of anticoagulants in treatment. Each case was classified on each occasion as a "satisfactory risk" or a "poor risk" according to the "uninstructed personal opinion of the doctor handling the case". Ten patients died within 24 hours of admission and were not further studied, and 50 others were excluded because the diagnosis was in some doubt. Of the remaining 107, the final classification (after 48 hours) was "satisfactory" in 59 and "poor" in 48 cases, 6 of the latter having been initially classified as "satisfactory" and 24 of the former

group having been originally classified as "poor" (of these, 3 died). Thus in 29% of cases the apparent prognosis changed in the first 48 hours. Of the 107 patients who survived the first 24 hours after admission, 15 (14%) died. Of the 59 classified in the "satisfactory-risk" category, 39 received anticoagulants and 2 of these died, while of the 20 receiving no anticoagulants, one died. Of the 48 patients in the "poor-risk" category, 43 received anticoagulants and 11 of these died, whereas of the 5 receiving no anticoagulants, one died. Thus with or without anticoagulants the mortality among "satisfactory-risk" cases was 5%, and among "poor-risk" cases 25%.

An analysis of these cases showed that the most important features in the history which indicate a poor prognosis are previous attacks of myocardial infarction and of heart failure, while the presence of severe shock or acute pulmonary oedema at the time of the attack is a bad sign. The general appearance of the patient was of great value in assessing the severity of the attack. Absence of changes in the QRS complex in the 12-lead electrocardiogram indicated a "satisfactory" risk. No deaths occurred in patients admitted more than 24 hours after the onset, presumably because they were not considered ill enough to be admitted immediately to hospital.

It is concluded that it is impossible to determine the prognosis accurately in the first 48 hours after an acute myocardial infarction and that anticoagulants should therefore be given initially in all cases and withdrawn subsequently when the prognosis is seen to be good. *C. Bruce Perry*

1258. **Chances for Survival in Acute Myocardial Infarction. Survey of the Acute Phase in 1,318 Patients**

H. I. Russek and B. L. Zohman. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **156**, 765–768, Oct. 23, 1954. 13 refs.

The mortality among patients with acute myocardial infarction has been variously stated to range between 35 and 65%, with an average of about 50%. The authors believe that this gives too gloomy a picture, and they have therefore analysed the records of 1,318 consecutive cases of myocardial infarction admitted to three New York hospitals in order to determine the survival rates for the period spent in hospital (3 to 6 weeks). Of this number 611 (46·4%) were classified as "good-risk" patients because of the absence of previous infarction, intractable pain, shock, cardiac enlargement, gallop rhythm, congestive failure, arrhythmias or conduction defects, and "other states predisposing to thrombosis"; the remaining 707 patients were classified as "poor risks".

In the "good-risk" group the mortality was 3·4%: in the "poor-risk" group (53·6% of the total) it was 60%, the incidence of thromboembolic complications being 11·5%. Mortality was higher among the older patients, a fact which the authors attribute to the higher incidence of severe attacks in the elderly. In view of the results of this study the authors advise a more optimistic prognosis for patients in the "good-risk" class. They suggest that the fact that half the deaths in this group occurred within 48 hours of the patient's admission is a measure of the danger from the psychical or physical trauma which often attends removal to hospital [but this may be doubted].

[The authors do not appear to favour the use of anticoagulants. No attempt was made to assess the more valuable long-term prognosis, nor to test the validity of the criteria chosen to indicate a "good risk". Many sufferers from infarction do not seek admission to hospital or do not survive to reach it.] *J. N. Agate*

1259. **Action of Triethanolamine Trinitrate in Angina Pectoris**

D. G. Friend, J. P. O'Hare, and H. D. Levine. *American Heart Journal* [*Amer. Heart J.*] **48**, 775–779, Nov., 1954. 10 refs.

Triethanolamine trinitrate, one of the newer compounds introduced as a long-acting coronary vasodilator, was used at the Peter Bent Brigham Hospital (Harvard Medical School), Boston, in the treatment of 7 patients with typical angina. The patients continued to take nitroglycerin sublingually as needed for the relief of attacks, but in addition they took capsules containing 2 mg. of the drug 4 times a day for a month, and then capsules containing 2 mg. of nitroglycerin and capsules of lactose, each for a further month; neither the patient nor the attending physician knew which preparation was being taken at any particular time. Records were made of the occurrence of attacks, and analysis of these observations suggested that neither triethanolamine trinitrate nor nitroglycerin in doses of 2 mg. 4 times a day by mouth was of any particular value in the treatment of angina. *James W. Brown*

CHRONIC VALVULAR DISEASE

1260. **Valvulotomy for the Surgical Relief of Aortic Stenosis**

W. H. Muller and M. Hyman. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **99**, 587–594, Nov., 1954. 5 figs., 10 refs.

The problems encountered in the surgical relief of aortic stenosis are briefly reviewed and 13 cases are reported in this paper from the University of California, Los Angeles. It is first pointed out that operation should be performed on all patients with aortic stenosis causing symptoms, the only absolute contraindications being a significant aortic reflux, "evidence of poor myocardial reserve", complete heart block, and acute rheumatism. In patients with congenital valvular disease evidence of left ventricular strain and enlargement is an indication for operation. Age is not necessarily a deterrent, but caution should be exercised in selecting patients over the age of 50. Calcification of the valve is not a contraindication; indeed calcified aortic valves are present in most cases.

The authors' technique for aortic valvotomy is as follows. The heart is approached by a left anterior

thoracotomy through the 5th interspace, with division of the costal cartilage. This approach is preferred to the sternal split because it exposes all chambers of the heart, readily permits access to the mitral valve in double lesions, and facilitates cardiac massage in cases of standstill. The pericardium is opened widely, and pressure measurements are taken across the aortic valve. The valvulotome (similar to Bailey's instrument) is then passed into the left ventricle through a stab wound made in an avascular area at the apex of the heart, which has previously been infiltrated with 1% procaine, the incision being controlled by a strong purse-string suture and a Rumel tourniquet. By placing a hand on the aorta just above the valve ring the end of the instrument can be felt passing into the aorta through the valve. The instrument is then expanded, when there is usually a sensation of sudden yielding. The cardiotomy is closed with interrupted silk sutures, pressures are again measured across the valve, and the chest closed, with provision for drainage.

The patients operated on were between 14 and 63 years of age, the majority being between 30 and 45. There was one operative death, that of a man of 63 who died from irreversible cardiac arrest during a retrograde approach to the valve through the innominate artery. Two late deaths occurred: one patient died from head injuries 9 months after operation, and one on whom mitral valvotomy and aortic valvotomy had been performed simultaneously died 3 months after operation from pulmonary embolism. The remaining 10 patients were followed up for 4 to 15 months, the results in 9 of them being regarded as good or excellent. One patient in whom the valvotomy was probably inadequate because of haemorrhage during the operation did not improve. A rise in aortic pressure and a fall in left ventricular pressure were observed in several of the patients after operation. In no case did significant regurgitation develop, and in most cases angina, dyspnoea on exertion, and fatiguability were relieved. There were 2 cases of double mitral and aortic valvotomy, and one in which aortic valvotomy was carried out during an operation for coarctation of the aorta. The authors consider that in patients with dual stenotic lesions the most " significantly affected " valve should be treated first. *A. M. Macarthur*

1261. **Mitral Valvulotomy through a Rubber Diverticulum**
W. W. L. GLENN, J. M. SHANNON, and L. N. TURK. *Annals of Surgery* [*Ann. Surg.*] **140**, 741–747, Nov., 1954. 3 figs., 5 refs.

The authors describe a method whereby access may be gained to a stenosed mitral valve and valvotomy performed in the absence of an adequate atrial appendage. The technique consists in creating an artificial appendage by direct suture of the open end of a small, rubber, glove-like " diverticulum " on to the atrial wall. The use of this technique in experimental surgery on dogs to gain safer entry into the left ventricle and aorta is also mentioned.

The advantages claimed for this procedure over a more direct approach to the operative area are: (1) that the technique can be made entirely bloodless; (2) that once in operation, the diverticulum allows slow and deliberate exploration and repair of cardiac defects, while the continuous infusion of heparin through one of the " fingers " of the rubber diverticulum minimizes embolus formation; and (3) that instrumentation through the diverticulum is easily carried out without excessive blood loss. *C. A. Jackson*

1262. **Rheumatic Crises Provoked by Mitral Commissurotomy.** (Les crises rhumatismales provoquées par la commissurotomie mitrale)
P. SOULIÉ, Y. BOUVRAIN, P. FORTIN, and —. CARAMANIAN. *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **70**, 879–896, Oct. 15, 1954. 11 refs.

Out of a total of 120 cases of mitral stenosis treated by commissurotomy and followed up for periods of 6 months to 3 years, the operation was considered to have caused a recurrence of acute rheumatism in 10, which are here reported fully. In 5 cases there was no past history of rheumatic fever and in 3 cases the last attacks were 30, 13, and 6 years respectively before the operation. The 2 remaining patients had had attacks more recently (3 and 7 months respectively before operation). The flare-up followed the operation after an interval of 3 weeks to 2 months.

The authors feel that some of their findings are open to criticism for various reasons, but they conclude with some confidence that the operation should not be carried out in any case in which a recent rheumatic flare-up has occurred, as it is likely that a further relapse will be provoked. Although this will not necessarily prove to be of a severe type, they feel that the risk should never be incurred. *W. S. C. Copeman*

SYSTEMIC CIRCULATORY DISORDERS

1263. **Low Thoracic–High Lumbar Sympathectomy for Vascular Diseases of the Legs**
R. P. HOHF, W. S. DYE, J. H. OLWIN, and O. C. JULIAN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **156**, 1238–1240, Nov. 27, 1954. 15 refs.

1264. **Chemical Quantitation of Epinephrine and Norepinephrine in Thirteen Patients with Pheochromocytoma**
W. M. MANGER, E. V. FLOCK, J. BERKSON, J. L. BOLLMAN, G. M. ROTH, E. J. BALDES, and M. JACOBS. *Circulation* [*Circulation (N.Y.)*] **10**, 641–652, Nov., 1954. 3 figs., 11 refs.

At the Mayo Clinic a slight modification of the fluorometric method of Weil-Malherbe and Bone for the quantitative estimation of adrenaline-like substances in plasma, particularly when combined with a provocative histamine test, has been found of value in the diagnosis of phaeochromocytoma. In 13 patients with phaeochromocytoma the plasma concentration of adrenaline-like substances was more than 4 μg. per litre and that of adrenaline and noradrenaline combined was more than

12 μg. per litre. To establish the diagnosis in some cases it was necessary to obtain blood during or shortly after a paroxysm of hypertension. Unfortunately, false high values were obtained in blood taken from patients with azotaemia [so the test has certain limitations].

G. B. West

1265. **Cerebral Hemodynamic Response to Blood Pressure Reduction with Phenoxybenzamine (Dibenzyline-688A)**

J. H. MOYER, H. SNYDER, and S. I. MILLER. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **228**, 563–567, Nov., 1954. 7 refs.

Cerebral blood flow does not appear to be regulated by the sympathetic nervous system, since stellate ganglion block does not affect it. However, there may be sympathetic fibres which traverse the ganglion and transmit impulses to cerebral vessels. The study described in this paper from Baylor University, Houston, Texas, was undertaken to determine whether there is any evidence for or against adrenergic activity being involved in the regulation of cerebral blood flow.

Phenoxybenzamine (" dibenzyline "), a potent adrenergic blocking agent, was given by continuous intravenous infusion to 7 patients with severe hypertension, the infusion being prepared by dissolving 1 mg. of the drug per kg. body weight in 300 ml. of 5% glucose. The infusion was administered at the rate of 4 to 6 ml. per minute until the blood pressure was normal. A dose of 0·2 mg. of noradrenaline was given to test for adrenergic blockade, and the infusion was discontinued when a reversal of effect (sharp fall in blood pressure) was obtained. The usual blocking dose of phenoxybenzamine was 0·50 to 0·75 mg. per kg. body weight. Cerebral blood flow was determined by the nitrous oxide method of Kety and Schmidt (*J. clin. Invest.*, 1948, **27**, 476).

As the blood pressure fell, cerebral blood flow was maintained by vasodilatation. When, however, the blood pressure fell to low normotensive or hypotensive levels the flow was depressed, but even then significant cerebral anoxia was not usually observed because there was increased extraction of oxygen from the blood flowing to the brain. There did not appear to be any preferential release of vasoconstriction in cerebral vessels as compared with those in the rest of the body.

Bernard Freedman

1266. **Hypertensive Retinopathy and Its Medical Treatment**

R. PLATT. *Quarterly Journal of Medicine* [*Quart. J. Med.*] 23, 441–450, Oct., 1954. 20 figs., 13 refs.

Writing from the University of Manchester, the author discusses the retinal changes found in hypertension. These may be considered under five headings, as follows. (1) The well-known vascular changes, such as narrowing and irregularity of the arterioles with compression of the veins. These changes are probably more closely related to the age of the patient and duration of the hypertension than to the height of the intra-arterial pressure. (2) Vascular accidents, such as retinal arterial or venous thrombosis, central or peripheral. Though probably usually related to hypertension, these accidents may occur in persons with normal blood pressure. (3) Hypertensive neuroretinopathy. This is a sign of the malignant phase of hypertension and is seldom found when the diastolic pressure is less than 140 mm. Hg. When there is associated nephritis and pyelonephritis it can occur in young people; otherwise the age of onset is usually between 40 and 55 years. The retina is seen to be oedematous, with " cotton-wool " exudates and haemorrhages; papilloedema is always present but may be masked by the general retinal oedema. In the author's view the development of this condition is an absolute indication for immediate hypotensive therapy to save vision. (4) Arteriosclerotic retinopathy. This condition, which is manifested by haemorrhages and " star " figures, occurs mainly in older people and carries a less grave prognosis than neuroretinopathy, but the two conditions often overlap. (5) Papilloedema may be present alone or appear before the other changes; if the diastolic pressure is much below 140 mm. Hg cerebral tumour should be strongly suspected.

Of 39 of the author's patients with retinopathy (details are given in a table), 17 were treated with hypotensive drugs, mainly with injections of " ansolysen " (pentapyrrolidinium bitartrate) or " ansolysen retard ", sufficiently long to achieve results. Excluding 3 cases too recent for evaluation, the remaining 14 were all improved. In the majority vision was restored to normal, the retina becoming clear in about 6 months. *C. W. C. Bain*

1267. **Evidence for Relationship between Sodium (Chloride) Intake and Human Essential Hypertension**

L. K. DAHL and R. A. LOVE. *Archives of Internal Medicine* [*Arch. intern. Med.*] **94**, 525–531, Oct., 1954. 15 refs.

Blood pressure and sodium chloride intake were studied in 547 members of the staff of the Brookhaven National Laboratory, Upton, New York, when they presented themselves for annual physical examination. Hypertension was considered to be present when the blood pressure exceeded 140/90 mm. Hg. Salt intake was regarded as " low " if the subject did not at any time add salt to food at table; if salt was added only after the food had been tasted and found insufficiently salt, the intake was regarded as " average "; when salt was added as a routine before the food was tasted the intake was defined as " high ". According to this classification, 65 subjects had a low intake, 243 an average intake, and 239 a high intake. The mean age of the patients in the three groups was similar, and it was noted that the mean blood pressure in the 3 groups was not significantly different.

None of the patients with a low salt intake had hypertension; of the patients with average and high intake, 17 and 24 respectively had hypertension. The correlation between salt intake and the presence of hypertension was thought to be significant. About half of the 41 hypertensive subjects were overweight or obese compared with 23% of those with a low salt intake and about one-third of those with an average or high intake.

The authors suggest that some minimum level of sodium intake must be exceeded before essential hypertension will develop, and that some other factors are concerned in its pathogenesis.

(In an addendum the authors state that the investigation has since been extended to include observations on a total of 897 subjects. Altogether, 98 had a low salt intake, 402 an average intake, and 397 a high intake. Hypertension was found in one patient with a low intake, in 30 subjects with an average intake, and in 40 with a high intake. The authors suggest that the significance of the earlier findings is supported by these additional observations.) *K. G. Lowe*

1268. **Treatment of Hypertensive Disease with Hydralazine. Comparison of Its Action with that of Low Sodium Diet in Hospitalized Patients**

A. J. STUNKARD, G. H. EURMAN, M. WACHSPRESS, and A. R. WERTHEIM. *American Journal of Medicine* [*Amer. J. Med.*] **17**, 712–721, Nov., 1954. 2 figs., 21 refs.

The comparative effects of administration of hydrallazine and of a low-sodium diet in the treatment of hypertension were studied at the Goldwater Memorial Hospital, New York. A total of 25 hypertensive patients received an average daily dose of 530 mg. of hydrallazine. The blood pressure "for the day" was the lowest of three readings taken an average of 2 hours after the first dose of the drug; this was estimated three times a week and the average taken as the "blood pressure level for the week". In 3 patients administration of the drug had to be discontinued because of side-effects. In 5 there was no blood-pressure response at all, and in the remainder there was a slight fall [the significance of which cannot be judged without details of spontaneous fluctuations in blood pressure during the control period]. Side-effects included an increase in headache and in cardiac damage. Comparison of these results with those of a low-salt regimen indicated that hydrallazine had a less beneficial influence on the hypertension.

J. McMichael

1269. **The Value of Rauwolfia Serpentina in the Hypertensive Patient**

F. A. FINNERTY. *American Journal of Medicine* [*Amer. J. Med.*] **17**, 629–640, Nov., 1954. 18 refs.

A study of the value of rauwolfia serpentina, alone and in combination with other more potent hypotensive drugs, is reported in this paper from Georgetown University, Washington, D.C. A total of 87 hypertensive patients were treated as follows: 44 received "rauwiloid", an extract of *Rauwolfia serpentina*, only; 22, who had previously been maintained on "veriloid", an extract of *Veratrum viride*, were given this drug again combined with rauwiloid; and 21 who were receiving hexamethonium or hydrallazine were given rauwiloid in addition. In patients with mild hypertension and nearly normal fundi who were given rauwiloid alone there was an average reduction in blood pressure of 20/18 mm. Hg. The results were less good in patients with more severe retinopathy, and in some cases the effect of rauwiloid did not become manifest for 3 to 4 months. When rauwiloid was given in combination with veriloid there was an average reduction in blood pressure beyond that achieved with veriloid alone of 9/7 mm. Hg. When rauwiloid was added to a regimen of hexamethonium or hydrallazine a significant reduction in the dosage of the two last-named drugs was possible in 18 of the 21 cases, with relief of the side-effects of methonium.

J. McMichael

1270. **Rauwolfia in the Treatment of Essential Hypertension**

R. W. WILKINS. *American Journal of Medicine* [*Amer. J. Med.*] **17**, 703–711, Nov., 1954.

In this paper from Massachusetts Memorial Hospitals and Boston University the author discusses many aspects of the use of rauwolfia and its derivatives in the treatment of essential hypertension. The tranquillizing action of rauwolfia, which was first used as a sedative in mental disorders, is accompanied by a fall in arterial pressure, a slowing of the pulse, and nasal congestion. Its "slow" action in reducing blood pressure in hypertensive patients may take 3 to 6 weeks to become apparent. Reserpine, the pure crystalline alkaloid of *Rauwolfia serpentina*, is recommended in a dosage of 0·1 mg. 4 times daily, this dosage being less likely to produce severe mental depression than a higher one. Rauwolfia potentiates the pressure-reducing action of other drugs, such as veratrum or methonium; it is of special value in the treatment of patients with mild labile hypertension. The author found that with reserpine there was an average fall of 24/15 mm. Hg compared with 10/4 mm. Hg with a placebo. More potent hypotensive agents are given in addition if the results are not sufficiently good, but the additive effect of rauwolfia is such that only small doses of the more powerful drugs are required. Subjective improvement in most hypertensive patients who are troubled by anxiety, irritability, and aggressiveness is striking. *J. McMichael*

BLOOD VESSELS

1271. **A Study of One Hundred and Sixteen Aneurysms of the Aorta and Iliac Arteries with Remarks Concerning Surgical Attitudes**

R. K. ZECH and K. A. MERENDINO. *American Surgeon* [*Amer. Surg.*] **20**, 1150–1161, Nov., 1954. 6 figs., 14 refs.

The ratio of aneurysms of syphilitic origin to those of arteriosclerotic origin, reported by Osler in 1905 to be 10 to 1, has changed markedly in the intervening half-century. In this statistical study the authors survey the incidence and type of aneurysm of the aorta and iliac arteries in 3,313 necropsies carried out at King County Hospital, Seattle, between 1946 and 1952. The series was selected in that it included an unusually large number of aged patients, the average age being 69 (range 40 to 89 years). Aneurysm was found in 116 cases (3·5%), 87 of the subjects being male and 29 female. The aneurysm was arteriosclerotic in 72 instances and syphilitic in 44 [elsewhere in the paper these figures are

given as 66 and 50 respectively] and in 62% of cases was diagnosed before death. All the patients, with one exception, were dead within 37 months of diagnosis of the lesion, regardless of its aetiology or site, the average survival time being 9 months. Prognosis was worst in cases of arteriosclerotic aneurysm with symptoms; in the syphilitic group aneurysm *per se* was the cause of death in only 16% of cases, the remaining patients dying of an associated cardiac or cerebral lesion.

Rupture occurred most commonly in saccular aneurysms of arteriosclerotic aetiology and was not prevented by the presence of laminated mural clot. Pain was the commonest symptom in both thoracic and abdominal lesions, mild abdominal pain often indicating a leak which did not proceed to rupture for some weeks. About half the patients with abdominal aneurysm complained of an abdominal mass; those with intrathoracic aneurysm complained of various symptoms due to pressure. Of aneurysms of the aortic arch, 95% were syphilitic, as were 75% of those of the descending aorta. In contrast, all the abdominal lesions were of arteriosclerotic origin.

The surgical treatment, which is briefly discussed, is divided into palliative treatment—consisting chiefly in the wiring technique and application of fibrosing agents—and curative treatment, that is, excision and grafting or excision and lateral repair. The method chosen must depend on the site of the aneurysm, only palliation being possible in most lesions of the ascending aorta and aortic arch, but excision may be employed for most aneurysms of the descending thoracic and the abdominal aorta below the level of the renal arteries. It must depend also on the general condition of the patient, in particular in respect of widespread vascular disease. As in most cases of abdominal aneurysm symptoms indicate impending rupture, excision and grafting is the method of choice in these cases in spite of the high risks of the operation. *A. M. Macarthur*

1272. **Coronary Disorders in Peripheral Arteritis.** (Les troubles coronariens au cours des artérites des membres) G. FAIVRE, C. PERNOT, and R. LAGARDE. *Presse médicale* [*Presse méd.*] **62**, 1515–1517, Nov. 6, 1954. 3 figs., 20 refs.

In a study of the relationship between coronary and peripheral arterial disease carried out at the Faculty of Medicine, Nancy, the examination of a random sample of 50 cases of endarteritis obliterans revealed an incidence of 28 cases of concomitant coronary artery disease; in 3 cases the evidence was clinical only, in 6 cases electrocardiographic only, and in 19 both. A little over one-third of the patients with coronary disease had signs of myocardial infarction or ischaemia.

Secondly, a group of 60 patients with either coronary disease or lower limb arteritis were studied and followed up. Of these, 42 had symptoms of coronary disease, 13 having suffered an acute attack, 13 having vague anginal pain, and 16 other symptoms only, such as dyspnoea of effort. In 18 cases the condition was "silent", signs of infarction, ischaemia, and bundle-branch block being seen on the electrocardiogram only. The authors stress the advantage of performing routine electrocardiography on patients with peripheral arteritis to reveal these silent cases.

When both coronary and peripheral arterial disease are present, peripheral disease usually appears first. Since atheroma is the basis of both diseases, the two conditions usually progress in a parallel manner with exacerbations and extensions of the process, although the coronary extensions may be silent. Sometimes exacerbations of one pain (cardiac or peripheral) may appear to ameliorate the other. There may also be progressive disease of other arteries, such as the cerebral or mesenteric. In the authors' series the commonest cause of death was an anginal crisis or cardiac insufficiency; in some cases death followed a cerebrovascular accident or mesenteric thrombosis. Treatment is not discussed, but the use of anticoagulants and also dietetic measures to reduce the atheroma are briefly mentioned.

D. Goldman

1273. **Periarteritis Nodosa: Recognition and Clinical Symptoms**

M. A. BLANKENHORN and H. C. KNOWLES. *Annals of Internal Medicine* [*Ann. intern. Med.*] **41**, 887–892, Nov., 1954. 6 refs.

On the basis of the pathological findings, 45 cases of necrotizing angiitis occurring at the Cincinnati General Hospital (University of Cincinnati) were divided into three groups. (1) In 21 cases the condition was designated "secondary" periarteritis nodosa and was found after a careful search in patients dying of hypertensive renal disease. (2) In 14 cases the typical Kussmaul–Maier type of periarteritis nodosa was present, in which the small and medium-sized arteries were involved and the lesions were situated at the points of branching, particularly in muscle. Lesions of various ages were found together and the condition was associated with vascular obstruction and hypertension. All organs in the body were commonly involved. (3) The remaining 10 were regarded as cases of hypersensitivity angiitis. Here the arterioles, venules, capillaries, and small arteries of the viscera and interstitial tissues were involved. All lesions appeared to be of the same age and showed an exudative reaction. Hypersensitivity angiitis was commonly associated with visceral interstitial inflammation, necrotizing glomerulonephritis, and fibrinoid pneumonia.

Peripheral eosinophilia was common in the cases of periarteritis nodosa and rare in those of hypersensitivity angiitis. Uraemia, rare in primary periarteritis, was common in hypersensitivity angiitis. In the cases studied primary periarteritis nodosa ran a long clinical course, whereas hypersensitivity angiitis was a fulminating disease with fever, skin rash, nephritis, and myocarditis, and there was a frequent history of exposure to some antigenic substance. It is concluded that primary periarteritis nodosa and hypersensitivity angiitis represent two distinct conditions. *C. Bruce Perry*

1274. **Trypsin Given Intramuscularly in Chronic, Recurrent Thrombophlebitis**

I. INNERFIELD. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **156**, 1056–1058, Nov. 13, 1954. 8 refs.

Haematology

1275. **Immunological Anaemia, Leucopenia, and Thrombocytopenia. Relationship between Antibodies against the Three Cellular Elements of the Blood.** (Anémies, leucopénies, thrombopénies immunologiques. Association d'anticorps dirigés contre les trois lignées cellulaires du sang)
J. BERNARD, J. DAUSSET, G. MALINVAUD, and G. LESUEUR. *Bulletins et mémoires de la Societé médicale des hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **70**, 651–667, June 11, 1954. 30 refs.

The authors describe in detail the case of a man aged 59 in whom antibodies against the erythrocytes, leucocytes, and platelets were detected. The man had always been healthy up to the time of a first episode of thrombocytopenic purpura with leucopenia in 1952. Fifteen months later a haemolytic anaemia developed. The techniques used for the detection of the antibodies are described and the relevant literature discussed. Although there have been several instances in which antibodies have been detected against two of the cellular elements of the blood, it is believed that this is the first instance of antibodies being found against all three elements in one patient. The possible aetiology is considered. Although in many of the reported cases auto-immunization appeared to be the most likely cause, in nearly every case the patient had had blood transfusion at some time previously, often before the detection of the presence of antibodies, so that the possibility of immunization could not be excluded. *R. F. Jennison*

1276. **The Total Amount of Haemoglobin and the Blood Volume in Polycythaemia Vera Treated with Radiophosphorus.** [In English]
H. WAHLUND. *Acta medica Scandinavica* [*Acta med. scand.*] **150**, 199–205, Oct. 30, 1954. 3 figs., 6 refs.

At Karolinska Sjukhuset, Stockholm, the total amount of haemoglobin and the blood volume were determined in 10 cases of polycythaemia vera before and after treatment with radioactive phosphorus (^{32}P). The patients (4 males and 6 females, aged 52 to 72 years) were given ^{32}P by mouth or intravenous injection in a dose of 5·1 to 7·0 millicuries, corresponding to 0·08 to 0·13 mc. per kg. body weight.

Before treatment the total amount of haemoglobin and the erythrocyte volume were approximately twice the normal; after treatment normal values were observed in two-thirds of the patients. The plasma volume in two-thirds of the cases was within normal limits both before and after treatment. However, there was a tendency to low plasma volume before the start of treatment; this was noted particularly in the remaining one-third of the cases, but these values also became normal after treatment with ^{32}P. Changes in the total blood volume were not of the same magnitude as those in the erythrocyte volume.

The author concludes that the haemoglobin level and the haematocrit reading do not provide a reliable basis for the determination in all patients of the degree of severity of polycythaemia. Further, similar doses of ^{32}P do not appear to have any effect on haemoglobin formation in haematologically normal individuals; thus erythropoiesis is considerably less sensitive to irradiation in normal subjects than in polycythaemic patients. He discusses the effect of ^{32}P on the bone-marrow mechanism, and inclines to the view that the bone marrow in polycythaemia reacts normally to the ordinary stimulating factors, but that additional haematopoiesis takes place, as in a neoplastic lesion, and that the ^{32}P acts as an inhibitor of the neoplastic process.

John F. Wilkinson

1277. **The Role of Sedormid in the Immunological Reaction that Results in Platelet Lysis in Sedormid Purpura**
J. F. ACKROYD. *Clinical Science* [*Clin. Sci.*] **13**, 409–423, Aug., 1954. 5 refs.

The author, at St. Mary's Hospital, London, has continued his investigation of the mechanism of purpura due to " sedormid ", in which he has shown (*Clin. Sci.*, 1951, **10**, 185; *Abstracts of World Medicine*, 1952, **11**, 166) that 4 factors are involved—platelets, sedormid, a lytic factor in the serum of sensitized patients, and complement. In all experiments sedormid was used in the form of a saturated solution in physiological saline, and complement fixation was the index of sedormid activity. Complement in the serum of sensitized patients was inactivated by heating at 56° C. for 20 minutes, unheated guinea-pig serum being subsequently used as necessary as the source of complement. Dialysis, when required, was carried out in " cellophane " sacs at 4° C., and a large excess of dialysing fluid was kept agitated by passing through it a stream of air.

The experiments described in this paper were undertaken to investigate the possible union of sedormid with either platelets or the serum factor. The results indicated that sedormid probably acts as a link between platelets and the lytic factor in the serum of sedormid-sensitive patients. Sedormid was, however, so loosely attached to the platelets that it could be dialysed from combination with the platelets and the lytic factor. Similar results were obtained with platelets from normal and sedormid-sensitive patients.

It is concluded that sedormid acts as a hapten, conferring antigenic properties on the platelets. The compound formed by the union of sedormid with platelets seems, however, to be extremely labile and can therefore be only weakly antigenic. It is postulated that this in itself explains the rarity of sedormid sensitivity, for only those whose immune reactions are stimulated by such a weak antigen will produce antibody and develop thrombocytopenia. *Mary D. Smith*

BLOOD TRANSFUSION

1278. **Changes in the Iso-antibody Characteristics of Group O and Group B Donors after Prophylactic Vaccines**
C. CONROY, M. SCHWARZ, and D. I. BUCHANAN. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **71**, 262–267, Sept., 1954. 4 refs.

The authors have followed up certain observations reported by Crawford *et al.* (*Lancet*, 1952, **2**, 219; *Abstracts of World Medicine*, 1952, **12**, 527), who showed that T.A.B. inoculation stimulated production of an anti-A haemolysin. In the present paper from Alberta, Canada, they report the results of tests carried out on the blood of 20 members of the Royal Canadian Air Force who had previously received inoculations of T.A.B. with tetanus toxoid (T.A.B.T.) or with tetanus and diphtheria toxoids (T.A.B.T.D.). Haemolysin tests were performed against Group-A_1 and Group-A_2 cells. Furthermore, agglutination tests were carried out in serial dilutions of O and B sera in normal saline and in AB serum; the indirect Coombs test was also performed. Out of 20 specimens of serum examined, 16 showed a strong haemolysin against A_1 test cells, and 14 were also haemolytic against A_2 cells. In some cases the anti-A titre was much higher when AB serum was used as a diluent in place of saline; this could be regarded as an indication of the presence of a probable immune anti-A agglutinin. It was also found that 14 to 18 days after a booster dose of 0·5 ml. of T.A.B.T.D. the titre in some cases increased up to 1:512,000 in AB serum. The results of the Coombs test also showed the immune characteristic of the specimens. The results obtained with 22 specimens of serum from civilian donors were, however, in marked contrast. None showed intense lysis of the test cells, and anti-A and anti-B titres were low; moreover, the result of the Coombs test was negative in 19 of the 22 specimens. It is suggested that for emergency purposes Group-O blood should be obtained only from civilian donors who have no recent history of inoculation. *Kate Maunsell*

1279. **Preservation of Red Cells for Blood-grouping Tests.** [In English]
H. CRAWFORD, M. CUTBUSH, and P. L. MOLLISON. *Vox sanguinis* [*Vox Sanguinis* (*Amst.*)] **4**, 149–154, Nov., 1954. 8 refs.

It is sometimes necessary or convenient to preserve for long periods the erythrocytes to be used for routine testing of patients' sera. In the study here reported from the Postgraduate Medical School of London, samples of blood containing the antigens A, B, M, N, S, P, C, c, D, E, K, Fy^a, Le^a, and Le^b were stored in various solutions at room temperature, at +4° C., and −20° C. Erythrocytes stored in acid citrate–dextrose (A.C.D.) mixture kept well for 3 days at room temperature and for more than 14 days at +4° C., although the reactions became weaker after 7 days. With erythrocytes stored for one year at −20° C. in trisodium-citrate–glycerol solution the reactions with blood-grouping sera were almost as good as those of fresh cells.

For preservation at −20° C. blood was taken into the A.C.D. mixture, centrifuged, and the supernatant removed and replaced by an equal volume of one of the following solutions: (1) glycerol (40%) and 5% trisodium citrate (60%); or (2) a mixture of 40% of glycerol and 60% of a solution containing 3·25% tripotassium citrate, 0·6% dipotassium hydrogen phosphate, and 0·47% potassium dihydrogen phosphate. For recovery the cells were thawed out, and washed in decreasing concentrations of glycerol (16%, 8%, 4%, and 2% in 3% citrate) and then three times in saline.

The authors point out that there is no close relation between the viability of cells from the point of view of transfusion and their reactivity with antisera on storage.
John Murray

ANAEMIA

1280. **The Practical Value of Electrophoresis (Tiselius's Optical Electrophoresis and Micro-electrophoresis on Paper) in the Diagnosis of the Hereditary Haemolytic Anaemias.** (L'intérêt pratique de l'électrophorèse (électrophorèse optique de Tiselius et micro-électrophorèse sur papier) pour le diagnostic des anémies hémolytiques héréditaires)
E. BENHAMOU, J. PUGLIÈSE, P. GRIGUER, and P. AMOUCH. *Presse médicale* [*Presse méd.*] **62**, 1513–1515, Nov. 6, 1954. 5 figs., 30 refs.

A brief account is given of the various abnormal types of haemoglobin found by means of electrophoresis in cases of hereditary haemolytic anaemia, and the diagnostic value is pointed out of comparing the mobilities of the various haemoglobins under electrophoresis in the Tiselius apparatus with phosphate buffer at *p*H 8·2 and with cacodylate buffer at *p*H 6·5. With the phosphate buffer the order of mobility of the haemoglobins is A>F>S>C>D, whereas with cacodylate mobility is greater in haemoglobins C and S, in that order, followed by haemoglobins A, F, and D with equal mobilities.

With the Tiselius apparatus and a phosphate buffer haemolysates of blood from carriers of the sickle-cell trait and patients with thalassaemia minor give a curve with a double peak, while in cases of sickle-cell disease and thalassaemia major the curve has only a single peak. With cacodylate buffer on the other hand heterozygotism is characterized by a double peak only in the case of the sickle-cell trait, the curve in both varieties of thalassaemia having a single peak. Filter-paper electrophoresis with veronal buffer at *p*H 8·6 gives the relative mobilities of the haemoglobins as A>F>S and D>C. A method for the preparation of haemolysates for testing by this method is outlined.

The value of haemoglobin electrophoresis is illustrated by four examples: (1) Singer's discovery of haemoglobin S in a carrier of the sickle-cell trait in whose blood the sickling phenomenon could not be demonstrated. (2) The distinction between thalassaemia syndromes and the variants of haemoglobin-C disease as causes of anaemia with target cells in the blood. (3) A case in which thalassaemia had been diagnosed clinically

in a fair-skinned Moslem woman with no negroid ancestry, but in whose blood electrophoresis disclosed the presence of haemoglobin S; further investigations then showed that she had sickle-cell disease. (4) A case in which 5 persons of a single family were thought to have associated thalassaemia syndromes on account of the presence of numerous target cells in the blood; no foetal haemoglobin being demonstrable in their blood by electrophoresis, further investigations were carried out which showed them to be suffering from favism.

It is urged that haemoglobin electrophoresis should be introduced as a standard method of investigation in all haematological laboratories.

[This paper contains little that is new, and one or two of the authors' interpretations are open to criticism. The references to sickle-cell disease and favism in Algiers are not without interest.] *A. J. Duggan*

1281. **Studies on Abnormal Hemoglobins. IX. Pure (Homozygous) Hemoglobin C Disease**
K. SINGER, A. Z. CHAPMAN, S. R. GOLDBERG, H. M. RUBINSTEIN, and S. A. ROSENBLUM. *Blood* [*Blood*] **9**, 1023–1031, Nov., 1954. 4 figs., 21 refs.

In this report from the Medical Research Institute (Michael Reese Hospital), Chicago, 4 cases of homozygous haemoglobin-C disease in negroes are described. The first patient, a male aged 22, had to undergo emergency appendicectomy, and splenomegaly was noted at operation. The second, a male aged 29, was admitted to hospital in 1948 and again in 1950 with acute pain and tenderness associated with an enlarged spleen; at the second admission splenectomy was performed. The third, a negro girl aged 11, had suffered attacks of abdominal pain about once a month for several years and had marked splenomegaly. The fourth patient, aged 9 and a sister of the preceding, was discovered on investigation of the family, but n symptoms except splenomegaly were noted. In all c ses blood examination showed evidence of a haemol tic process and the presence of large numbers of target cells.

Haemoglobin analysis was performed by standard electrophoretic methods at *p*H 6·5 and paper electrophoresis at *p*H 8·6. With either technique haemoglobin C was demonstrated as a single component in all cases. With the alkali denaturation technique no abnormal amounts of haemoglobin F were found. Seven other members of the family of the 2 female patients were studied, and since the parents were both carriers of the haemoglobin-C trait the results supported the postulate that pure haemoglobin-C disease results from the mating of persons harbouring the gene for haemoglobin C.

Erythrocyte survival time was determined by transfusion of 200 ml. of blood from the second patient. The mean cell life was 13 days, and all the transfused cells had disappeared by the 50th day. The elimination curve indicated a heterogeneity of the erythrocyte population which could not be due to the abnormal haemoglobin C, thus suggesting that some other erythrocyte constituent also influences cell survival.

In the authors' opinion splenectomy should be considered when marked thrombocytopenia accompanies pure haemoglobin-C disease, or when the enlarged spleen is producing pressure symptoms. In the second patient splenectomy did not reduce the haemolytic process. Since it has been calculated that 2% of the 15 million negroes in the U.S.A. are carriers of the haemoglobin-C trait, it seems likely that the homozygous disease will be recognized more frequently in the future.

A. J. Duggan

1282. **Studies on Abnormal Hemoglobins. X. A New Syndrome: Hemoglobin C–Thalassemia Disease**
K. SINGER, A. P. KRAUS, L. SINGER, H. M. RUBINSTEIN, and S. R. GOLDBERG. *Blood* [*Blood*] **9**, 1032–1046, Nov., 1954. 5 figs., 35 refs.

The authors describe a severe thalassaemic syndrome in a 33-year-old male negro admitted to the Michael Reese Hospital, Chicago. The patient's brother was found to be a carrier of the haemoglobin-C trait, and this discovery prompted investigation of all surviving members of the family. (The brother's own history is not without interest. His wife was a carrier of the sickle-cell trait and his 2 sons have sickle-cell–haemoglobin-C disease.)

The mother of the family had 77·4% of haemoglobin C, the remaining erythrocyte constituent being normal adult haemoglobin. The M.C.V. and M.C.H. of her erythrocytes were decreased, but the M.C.H.C. was normal; there was a reticulocytosis, and a few nucleated erythrocytes and 43% of target cells were present in the blood film. The authors conclude that the microcytic erythrocytosis points to a mild thalassaemia syndrome, and that the mother was therefore suffering from haemoglobin-C–thalassaemia disease.

Apart from the patient and his brother, 7 other children of this mother were examined. One daughter had an almost identical haematological picture to that of her mother, except that a small amount of foetal haemoglobin was present as well as 74·1% of haemoglobin C; this subject was also regarded as suffering from haemoglobin-C–thalassaemia disease. Another daughter showed the characteristics of the uncomplicated haemoglobin-C trait, while a third suffered from a severe form of thalassaemia similar to that of the propositus, her brother. Two further daughters showed mild thalassaemic manifestations, one had a mild hypochromic anaemia not unquestionably due to thalassaemia, and the last showed no haematological abnormality. The father of the family was dead. Almost all the haemolysates from the members of this family which did not contain haemoglobin C contained an unidentified component, demonstrable as a "shoulder" on the curves produced by standard electrophoresis in the Tiselius apparatus at *p*H 6·5. The mobility of this component, which was not necessarily a pigment, was faster than that of haemoglobin A, but definitely slower than that of haemoglobin C.

The authors classify the thalassaemic syndromes into thalassaemia major, thalassaemia intermedia, thalassaemia minor, microcytic erythrocytosis, and thalassaemia minima—in descending order of clinical severity. Thalassaemia major is regarded as a homozygous manifestation, and may result from the mating of bearers of

any type of thalassaemia. The original patient and one of his sisters were considered to have thalassaemia intermedia. The 2 sisters with mild thalassaemic syndromes were regarded as suffering from microcytic erythrocytosis.

The haemolytic anaemias produced by the combination of sickle-cell anaemia with thalassaemia are contrasted with the benign microcytic erythrocytosis of the 2 individuals with haemoglobin-C–thalassaemia disease. Since 2 other members of the family showed a similar blood picture but without the presence of haemoglobin C, this pigment evidently plays no significant role in producing the haematological picture of haemoglobin-C–thalassaemia disease. The simultaneous occurrence of the two abnormalities does not enhance the production of foetal pigment. The only abnormal manifestation of thalassaemia minima may be the increased resistance of the erythrocytes to hypotonic saline solutions—a phenomenon which is related to leptocytosis. Since leptocytosis also occurs in the haemoglobin-C trait the osmotic fragility test is no longer diagnostic and should therefore be supplemented by haemoglobin analysis when thalassaemia minima is suspected.

Although the mother of this family was heterozygous for the haemoglobin-C and thalassaemia genes, one of her daughters had no haematological abnormality. Hence, regardless of the genetic constitution of the father, it is clear that the genes for haemoglobin C and thalassaemia are not allelomorphs and segregate independently.

[Only the main issues arising from this study are indicated. Perusal of the original article is recommended to students of the haemoglobinopathies and human genetics.] *A. J. Duggan*

1283. **Thalassemia–Hemoglobin C Disease. A New Syndrome Presumably due to the Combination of the Genes for Thalassemia and Hemoglobin C**
W. W. Zuelzer and E. Kaplan. *Blood* [*Blood*] **9,** 1047–1054, Nov., 1954. 7 figs. 12, refs.

A male negro child was first seen at the Children's Hospital of Michigan (Wayne University College of Medicine), Detroit, at the age of 6 years with severe anaemia of unknown duration. There was no evidence of either blood loss or dietary deficiency, and iron therapy conferred no benefit. The child was thin and the mucosae pale, but there was no cardiomegaly and neither liver nor spleen was palpable. The erythrocytes showed marked variation in size, shape, and staining, the majority being target cells, some of which contained basophil inclusions. No nucleated erythrocytes were seen in the peripheral blood, the granulocytes and platelets were normal, and no sickling phenomenon was present. The osmotic fragility curve showed that some cells were unusually fragile and some unusually resistant. The marrow showed erythroid hyperplasia with a few cytoplasmic inclusions in the normoblasts.

The blood pictures of the patient's mother, twin sister, and 2 maternal half siblings were almost identical with one another, consisting partly of round, well-filled erythrocytes and partly of target cells, microcytes, fragments, and oval and elliptical cells; these were interpreted as expressions of thalassaemia minor. The father's blood contained 10 to 20% of target cells. Four other maternal half-siblings were haematologically normal. Haemoglobin studies showed that the mother and twin sister had normal haemoglobin A, while the patient and his father had a mixture of haemoglobins A and C. Less than 2% of alkali-resistant haemoglobin F was present in the blood of the patient and his mother.

Asserting that the thalassaemic syndromes are recognized only on essentially morphological grounds, the authors deduce that the patient inherited the haemoglobin-C gene from his father and the thalassaemia gene in single dose from his mother. Singly, the traits which these genes confer are relatively benign, but their interaction appears to have produced a severe anaemia with a distinctive blood picture.

[This case contrasts with the asymptomatic examples of the same genetic combination described by Singer *et al.* (see Abstract 1282).] *A. J. Duggan*

1284. **The Pathogenesis of Anaemia in Diseases of the Gastrointestinal Tract.** (К вопросу о патогенезе малокровия при поражениях желудочнокишечного тракта)
G. A. Alekseev. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **32,** 15–24, Nov., 1954. 11 refs.

In the author's opinion it is not an exaggeration to state that the majority of anaemias met with by the clinician are associated with some disturbance in the gastrointestinal tract. Such anaemias are, for example, pernicious anaemia, idiopathic hypochromic anaemia, the anaemia of sprue, and that associated with polyposis and carcinoma of the stomach.

The gastric (intrinsic) anti-anaemic factor of Castle has been identified by Glass as a mucoprotein which is present in the stomach of all persons except those suffering from pernicious anaemia. In the latter disease the extrinsic factor, vitamin B_{12} (cyanocobalamin), which is secreted from the fundal portion of the stomach and not, as was believed by Meulengracht, from the pylorus, produces remission when given by injection, but not when given by mouth unless accompanied by gastric mucoprotein. The author considers that the function of the mucoprotein is to protect cyanocobalamin from the intestinal microorganisms which would otherwise utilize it for their own metabolism. Thus the gastric mucoprotein is only a vehicle, protecting cyanocobalamin and enabling it to be assimilated and utilized. If it is absent cyanocobalamin can be utilized directly only if given parenterally.

Iron-deficiency anaemia may be associated with achylia gastrica, when it results from deficient ionization of iron because of the absence of free hydrochloric acid. This may occur after gastroenterostomy, for example, owing to regurgitation of alkaline intestinal juice into the stomach. In addition to true achylia gastrica, functional achylia may occur in such conditions as polyposis, carcinoma, syphilis, or gastritis associated with uraemia, all of which are associated with disturbance of fundal activity. The author describes a case of such an anaemia developing in a young man 5 years after the

performance of oesophago-enterostomy for stenosis of the oesophagus, with exclusion of the stomach from the digestive tract.

Severe enteritis may cause an anaemia of the macrocytic type; this is seen in pellagra, sprue, and polyposis, or strictures of the small intestine, conditions which interfere with absorption of the specific factor. The tapeworm *Dibothriocephalus* also causes a macrocytic anaemia in a small proportion of cases in which there is a latent insufficiency of gastric or hepatic anti-anaemic function. Less well understood are the iron-deficiency anaemias associated with pathological conditions of the bowel which interfere with the absorption of iron or of its combination to form ferritin. A case is described in which this type of anaemia developed after extensive resection of the small bowel for volvulus. Gastro-colic fistula as an aetiological factor in the production of iron-deficiency anaemia is well known.

The role of the bile in the assimilation of vitamin K is another example of the role played by the gastrointestinal tract in haematopoietic processes. Finally, the suggested specific role of pancreatic juice in the extraction from the products of digestion of the so-called thrombopoietic factor awaits confirmation.

L. Firman-Edwards

NEOPLASTIC DISEASES

1285. **Further Experience with "Sanamycin" [Actinomycin C] in the Treatment of Hodgkin's Disease.** (Weitere Erfahrungen mit Sanamycin bei der Behandlung der Lymphogranulomatose)
G. SCHULTE. *Strahlentherapie* [*Strahlentherapie*] **94**, 491–496, Aug., 1954. 1 fig.

The therapeutic effects of actinomycin C ("sanamycin") in the treatment of 100 histologically proved cases of Hodgkin's disease are here reported from Knappschaft Hospital, Recklinghausen, Westphalia. The drug was given by intravenous injection in doses of 100 μg. in the morning and 200 μg. in the evening to a total of 5,000 to 10,000 μg., and caused no untoward constitutional symptoms and there were no signs of ill effects on the haematopoietic system, liver, or kidneys. In 43 cases, 17 of them previously untreated, actinomycin C alone was given, but in the remainder it was supplemented by *x* irradiation, urethane, nitrogen mustard, or cortisone. After one course 10 of the 17 previously untreated patients were free from signs and symptoms and remained well for periods up to 18 months, those of working age being able to return to employment. Of the previously treated cases 4 died, and in most of the others remissions were shorter. In 57 cases the beneficial effect of sanamycin was slightly enhanced, particularly in previously untreated cases, by the addition of *x* irradiation or cortisone.

In general the best effects in all groups occurred in patients with only superficial lymph-node enlargement, no pyrexia, no gross blood changes, and no significant increase in the erythrocyte sedimentation rate; the least favourable results were obtained in cachectic, febrile patients with anaemia, splenomegaly, and raised sedimentation rate. The author points out, however, that sufficient time has not yet elapsed to assess the effect on ultimate prognosis.

Mary D. Smith

1286. **Leukaemia and Pregnancy**
J. ALLAN. *British Medical Journal* [*Brit. med. J.*] **2**, 1080–1082, Nov. 6, 1954. 15 refs.

The incidence and the effect of leukaemia in pregnancy are discussed and 4 new cases are reported in this paper from the Western Infirmary, Glasgow. Reviewing the literature, the author points out that of 34 cases of acute leukaemia complicating pregnancy, only in 2 was the disease diagnosed before pregnancy began; in most of the remainder it was diagnosed at 7 months. As would be expected, all the patients died—4 during pregnancy, 5 during parturition, and the remainder mostly within 14 days of delivery. There were 7 cases of severe postpartum haemorrhage. Foetal mortality was 60%, the majority of the deaths occurring before birth.

In most of the 61 reported cases of chronic leukaemia the disease was diagnosed before the onset of pregnancy. One patient died during pregnancy, 3 during parturition, and 17 within a year of delivery. Foetal mortality was 37·5%, the deaths being divided about equally between prematurity and stillbirth.

As regards the effect of pregnancy on the course of leukaemia, the author states that acute leukaemia runs its usual short course and pregnancy cannot be said to accelerate death. In chronic leukaemia, however, there is some evidence that pregnancy causes an acute exacerbation, especially in the rare case of a second pregnancy. There is no evidence that leukaemia is transmitted to the foetus.

R. F. Jennison

1287. **A Contribution to the Clinical Study of Pulmonary Involvement in Leukaemia.** (Contributo allo studio clinico delle localizzazioni polmonari nella leucemia)
I. CATTANEO and L. VERCILLO. *Haematologica* [*Haematologica*] **38**, 1021–1064, 1954. 12 figs., 43 refs.

The authors discuss the apparently rare condition of pulmonary involvement in leukaemia, with frequent references to the literature and with special reference to 2 cases of chronic lymphatic leukaemia and one of acute myeloblastic leukaemia, all with pulmonary involvement, seen at the General Medical Clinic, University of Pavia. In the first case of lymphatic leukaemia radiography showed an accentuation of the lung shadow suggestive of interstitial-tissue involvement, several areas of parenchymal infiltration, and elevation and fixation of the left dome of the diaphragm. In the second case numerous radiographs taken between 1949 and 1953 showed various degrees of opacity of the lung fields and changes in the hilar shadow. The case of blastic leukaemia was not examined radiologically and the pulmonary involvement was detected only when the lungs were examined at necropsy.

The diagnosis in these cases is far from simple. It is often difficult to decide whether the pulmonary involvement is due to the leukaemic process itself or to a superimposed bronchopneumonia. But the regression of the

pulmonary lesion concurrently with improvement in the blood picture under antileukaemic treatment, and absence of pyrexia, support the former possibility; moreover the cough is persistently dry and irritative, and there is in addition no response to antibiotic treatment. The second case had been treated with PAS until the bronchopneumonia-like appearances were recognized to be due to leukaemic involvement. In this case, however, a superimposed pyogenic infection could not be ruled out; in the course of the 4 years of observation bronchiectasis of gradually increasing severity developed in this patient.

The authors believe that pulmonary involvement in leukaemia is not so rare as the scarcity of reports of it would suggest. Clinically the cases are extremely difficult to distinguish from non-leukaemic pulmonary lesions; radiologically, miliary or submiliary, band-like, bronchopneumonic or lobar involvement can be seen; the symptomatology closely follows this anatomical distribution of lesions. The radiological aspect of these lesions is discussed at length. It is suggested that radiography of the chest should be carried out as a routine in all cases of leukaemia. The treatment of the condition is that of the leukaemia, but there is a place for the prophylactic use of broad-spectrum antibiotics in order to prevent the development of infective complications.

Ferdinand Hillman

1288. **Clinical Evaluation of 6-Mercaptopurine in the Treatment of Leukemia**

J. H. Burchenal, D. A. Karnofsky, M. L. Murphy, R. R. Ellison, M. P. Sykes, C. T. C. Tan, A. C. Mermann, M. Yuceoglu, and C. P. Rhoads. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **228**, 371–377, Oct., 1954. 5 figs., 9 refs.

The value of 6-mercaptopurine in the treatment of 269 patients with neoplastic diseases is discussed in this paper from the Sloan Kettering Institute, New York, the authors' patients including 140 with acute leukaemia, 8 with subacute leukaemia, 18 with chronic myelocytic leukaemia, and 4 with chronic lymphocytic leukaemia [the disease condition of the remaining patients is not stated]. The usual daily dose was 2·5 mg. per kg. body weight continued indefinitely; with this dosage the maximum effect was not usually manifest for 3 to 8 weeks. The treatment was of no value in chronic lymphocytic leukaemia, Hodgkin's disease, the reticuloses, or metastatic carcinoma. In 11 out of 12 patients in the early stage of chronic myelocytic leukaemia clinical and haematological remissions were noted. More than 50% of children with acute leukaemia obtained remission; some of the patients ultimately became resistant to the drug, but there was no cross-resistance to amethopterin or cortisone. On the other hand, only about one-third of the adults with acute leukaemia benefited.

The authors state that in the treatment of acute leukaemia 6-mercaptopurine or amethopterin is the drug of choice, ACTH and cortisone being reserved for emergencies, when rapid action is essential. In their experience combined therapy has not been more satisfactory than "sequential" use of these drugs. *P. C. Reynell*

1289. **Myeloblastic Leukaemoid Myelophthisis.** (La myélophtisie leucémoïde myéloblastique)

G. Mayer. *Annales de médecine* [*Ann. Méd.*] **55**, 561–584, 1954. 25 refs.

Writing from the Blood Transfusion Centre, Strasbourg, the author reviews in some detail those cases that present with more or less severe aplasia of the bone marrow but ultimately show appearances suggestive of, or even identical with, myeloblastic leukaemia. In agranulocytosis immature myeloid cells may be found in the marrow and occasionally erupt into the blood, representing a sort of perverted regeneration. The author points out that these cases are often misdiagnosed because histological examination of the morphology of the marrow is not employed to supplement the mainly cytological findings obtained from smears, which may be grossly misleading; he therefore advocates marrow biopsy rather than simple puncture with aspiration.

Myeloblastaemia and medullary myeloblastosis should not always be considered as being due to leukaemia—they may be due to leukaemoid myeloblastic myelophthisis. In the former, the primary process consists in cellular proliferation with arrest of maturation, whereas in the latter the process is primarily one of marrow destruction followed by hyperplasia and anaplasia. It is also recalled that myeloblastaemia may occur in the course of chronic myeloid leukaemia as the result of a sort of secondary anaplasia. Again purely reactive myeloblastosis may be present; this appears to be of toxic or infective origin, and usually disappears rapidly.

A. Piney

1290. **Classification of the Leukoses.** (Классификация лейкозов)

M. S. Dul'tsin. *Терапевтический Архив* [*Ter. Arkh.*] **26**, 3–10, Nov.–Dec., 1954. 8 refs.

The author discusses the problem of classification of the leucoses [with reference to the work of Russian authors only] and proposes the following scheme based on cytological grounds.

(1) *Reticuloses*, in which the affected cell is the haemohistoblast, the transformed cell of the reticular syncytium of the stroma of the haematopoietic organs. The reticuloses are further divided into two sub-groups: (*a*) forms in which there is a definite, destructive, malignant growth, such as reticulosarcoma, lymphosarcoma, lymphogranulomatosis, myelomatoses, and chloroma; and (*b*) acute, subacute, and chronic aleukaemic forms.

(2) *Haemocytoblastoses*, acute and subacute, affecting the parenchymatous cells of the haematopoietic organs, the haemocytoblasts. Again two sub-groups are recognized: (*a*) myeloses, which are of three types involving different cells, namely, acute (myeloblast), subacute (myeloblast, promyelocyte, and myelocyte), and chronic—aleukaemic or leukaemic—(myeloblast and unripe granulocyte); and (*b*) lymphadenoses, which are of two types, namely, acute (lymphoblast, prolymphocyte), and chronic—aleukaemic or leukaemic—(lymphocyte, prolymphocyte). In exacerbations of chronic lymphadenoses, however, more primitive cells appear, including haemocytoblasts as well as lymphoblasts and prolymphocytes.

H. W. Swann

Respiratory System

1291. **The Effect of Proteolytic Enzymes on the Physical and Chemical Characteristics of the Tracheobronchial Secretions of Patients with Poliomyelitis**
S. KOFMAN, M. H. LEPPER, G. G. JACKSON, and H. F. DOWLING. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **228**, 426–431, Oct., 1954. 9 refs.

Concerned with the frequency of atelectasis in patients with poliomyelitis and respiratory paralysis who had been subjected to tracheotomy, the authors, at the Municipal Contagious Diseases Hospital, Chicago, studied the effect of administration of proteolytic enzymes, which has been advocated by others as a means of increasing the fluidity of bronchial secretion and so facilitating its removal.

Aerosols of trypsin and of streptokinase and streptodornase were given to a small group of such patients, isotonic sodium chloride solution being used as a control. It was found that trypsin, which acts mainly by mucolysis, had no effect on the volume, *p*H, or amount of sediment in the secretion but caused a decrease in the viscosity, the effect lasting only 2 hours. With the streptococcal enzymes, which act mainly by fibrinolysis, a decrease in the viscosity and an increase in the volume of the secretion lasting about 4 hours were observed. No digestive action of the streptococcal enzymes was demonstrated. *A. Gordon Beckett*

1292. **The Use of Trypsin or Streptokinase–Streptodornase for the Therapy and Prevention of Atelectasis**
S. KOFMAN, M. H. LEPPER, G. G. JACKSON, and H. F. DOWLING. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **228**, 432–439, Oct., 1954. 5 figs., 7 refs.

In continuation of the investigation described in Abstract 1291 the authors report a controlled clinical trial to compare the effects of aerosols of trypsin, the streptococcal enzymes, and a non-protein solution in the prevention and treatment of atelectasis in 24 patients with poliomyelitis who had been subjected to tracheotomy and placed in a mechanical respirator. Trypsin appeared to facilitate aspiration of secretion but had no other effect; no favourable effect was obtained with the streptococcal enzymes. There were no adverse reactions in patients receiving trypsin or saline, but half the patients treated with streptococcal enzymes experienced severe reactions, including one who developed pneumonia.

Trypsin solution was instilled directly into the bronchial tree in 11 cases (21 instillations). In 2 cases pneumonia or atelectasis cleared, while in 8 there was improvement in the general condition. Bronchorrhoea occurred 11 times, and as a result frequent suction and constant observation were necessary. On 11 occasions the instillation was accompanied by side-reactions, usually within 30 minutes, the chief being dyspnoea, choking sensations, and retrosternal pain. These reactions were usually mild and did not interfere with treatment, but in a few cases they were severe and aspiration revealed bronchorrhoea. Antihistamine drugs did not appear to influence the incidence of side-effects.

While the improvement resulting from administration of trypsin was not statistically significant, the authors nevertheless consider that a trial in a larger series of cases might be worth while. *A. Gordon Beckett*

1293. **An Experimental Study of the Venous Collateral Circulation of the Lung. I. Anatomical Observations**
A. HURWITZ, M. CALABRESI, R. W. COOKE, and A. A. LIEBOW. *American Journal of Pathology* [*Amer. J. Path.*] **30**, 1085–1115, Nov.–Dec., 1954. 17 figs., 22 refs.

The pulmonary veins of an entire lung can be ligated without producing hemorrhage and necrosis, provided that the animals are protected with antibiotics; streptomycin in combination with penicillin appears to be more favorable in this regard than the latter alone. This observation suggests a contribution of infection to what has formerly been considered merely infarction.

After ligature of the pulmonary veins there develops a collateral circulation capable of carrying up to at least 20% of the blood flow were the venous drainage intact, and the oxygen content of the azygos blood rises. In part, this collateral circulation depends upon the expansion of pre-existing bronchial venous channels, probably in response to mechanical factors, and, in part, upon the development of new channels of large size from the capillaries of granulation tissue within pleural adhesions. Some of these supplement the hilar bronchial veins, but others join the pulmonary veins, end to end, at the periphery. The factors guiding this junction are not known, but in their discovery may lie an important key to the mechanisms of collateral circulation in general. The arterial collateral circulation is not altered concomitantly.

Since, in consequence of ligature of the pulmonary veins, expanded collateral veins of a lung can be caused to drain oxygenated blood via the azygos and innominate veins into the right heart, this operation suggests itself as a simple procedure possibly applicable to the partial correction of the disturbed hemodynamics of congenital transposition of the great vessels.—[Authors' summary.]

1294. **Lung Cancer and Common Inhalants**
E. C. HAMMOND. *Cancer* [*Cancer (N.Y.)*] **7**, 1100–1108, Nov., 1954. 8 figs., 21 refs.

The great reduction in the death rate over the last 50 years means that for every 1,000 men aged 50 in 1950 there were 182 who would not have lived to that age had they been born in 1870. Moreover, 40 of the 182 would have died of pneumonia, influenza, or pulmonary tuberculosis. Consequently a representative group of men aged 50 in 1950 is not truly comparable with a

similar group of men aged 50 in 1920, and it cannot be assumed that the two groups were equally susceptible to cancer of the lung in any investigation into the causes of the increased incidence of that disease between 1920 and 1950.

Fumes and dust produced by oil furnaces, motor vehicles, bituminous road surfaces, and cigarettes might all be held responsible for this increased incidence, since exposure to all has become more prevalent during the period; on the other hand smoke from coal is unlikely to be alone responsible, since coal consumption has not increased. Laboratory evidence shows that all the inhalants referred to are capable of causing cancer under suitable conditions, but the sum of the evidence is no more than suggestive and it does not follow that any of them causes cancer in man. Similarly although cigarette smoke is bactericidal to *Proteus vulgaris* and to Type-1 pneumococci *in vitro*, it does not necessarily follow that the increase in cigarette smoking is the cause of the reduced mortality from pneumonia.

Studies of the past smoking habits of patients with and without cancer of the lung add to the evidence that these habits are related to the development of the disease, but leave in doubt the degree of that association. In the author's opinion, if follow-up studies of the cause of death among persons whose smoking habits have previously been defined confirm the conclusions arrived at by the other method, " then there will be sufficient evidence to conclude beyond a reasonable doubt that cigarette smoking increases the probability that an individual will develop lung cancer ". *R. Doll*

1295. **Tobacco as a Cause of Lung Cancer. With Special Reference to the Infrequency of Lung Cancer among Non-smokers**

E. L. WYNDER. *Pennsylvania Medical Journal* [*Penn. med. J.*] **57**, 1073–1083, Nov., 1954. 28 refs.

Whereas it may be difficult for a patient to recall the exact amount of tobacco smoked over a long period, it is not difficult for him to state whether or not he has always been a non-smoker. A clear differentiation can therefore be made between smokers and non-smokers, and in view of the possible relation between smoking and cancer of the lung the present author has made a special study of the cases of lung cancer occurring in non-smokers in a series of 1,104 proved cases of the disease seen at the Memorial Center, New York, and in other series reported in the literature.

The principal finding in the author's series was that non-smokers formed a higher proportion of patients with adenocarcinoma (6 out of 60 men, or 10%, and 21 out of 25 women, or 84%) than of those with epidermoid, oat-cell, or anaplastic carcinoma (14 out of 979 men, or 1·4%, and 16 out of 40 women, or 40%). Moreover, the proportions of non-smokers among male and female patients with adenocarcinoma are close to those found in control groups of patients with other diseases or drawn from the general population. The high proportion of adenocarcinoma among the male non-smokers in the series (6 out of 20, or 30%) is supported by data collected from five other investigations (7 out of 28, or 25%). Of the 14 male non-smokers in the author's series with cancer of epidermoid or analogous types, 9 had been employed in an occupation suspected of carrying an increased risk of the disease (2 painters, 2 exposed to metal dust, 2 to petrol and oil fumes, 2 to wood dust, and one to arsenical insecticides). A similar incidence of occupational exposure to risk has been recorded among non-smokers in other series. No correlation was found between the place of residence and the histological type of the disease among non-smokers.

The main evidence relating lung cancer to smoking is reviewed and the conclusion reached " that the established statistical association between smoking and lung cancer is also a causative one ". *R. Doll*

1296. **Epidemiologic Studies on Smoking in Relation to Lung Cancer**

E. C. HAMMOND. *Pennsylvania Medical Journal* [*Penn. med. J.*] **57**, 1084–1087, Nov., 1954. 9 refs.

The evidence showing a connexion between cigarette smoking and cancer of the lung is summarized, and it is concluded that the increase in cigarette smoking has caused an increase in the incidence of the disease. The author suggests that before preventive action can be taken it is important to assess what other effects smoking may have. An important factor is that smoking gives pleasure to many people, and any attempt to interfere with that pleasure is likely to be resented and resisted. A happier solution than prohibition, therefore, would be to make smoking safe. This is a complex problem, since there is evidence that smoking increases the death rate from cancer of other sites and from coronary thrombosis as well as from lung cancer, and more than one noxious factor may be involved—say, one carcinogenic and one (? nicotine) causing coronary thrombosis.

It appears that cigar and pipe smoking have little or no relation to coronary thrombosis and much less effect on the death rate from cancer than cigarette smoking. This may be due to differences in the method of combustion, in the extent to which the smoke is inhaled, or in the type of tobacco used. In the author's view the most promising line of research is that directed towards the development of a harmless type of tobacco, rather than towards the removal of the carcinogenic agents from a noxious type. *R. Doll*

1297. **Cancer of the Lung. A Review of Experiences with 1,475 Cases of Bronchogenic Carcinoma**

A. OCHSNER, C. J. RAY, and P. W. ACREE. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **70**, 763–783, Nov., 1954. 23 figs., 6 refs.

The authors of this paper from the Ochsner Clinic and Tulane University, New Orleans, review their findings in 1,457 cases of bronchogenic carcinoma. Histological examination of the tumours showed that 49% were epidermoid carcinomata, 31% were undifferentiated, and 19% were adenocarcinomata. In 56% of the cases the tumour arose in one or other of the upper lobes—the left in 29% and the right in 27%. In most cases the presenting manifestation was lower respiratory tract infection or a viral pneumonia, other common presenting

symptoms being a change in the character of a chronic cough, haemoptysis, thoracic discomfort, or wheezing of recent onset. There was an average delay of 8½ months between the onset of the first symptom and the institution of treatment. The condition was diagnosed on bronchoscopy in only 33% of cases, but in 68% a positive diagnosis was reached on cytological examination of the sputum. In the authors' view the latter is the most valuable diagnostic aid in bronchogenic carcinoma. [The incidence of false positive results is not stated.] In 20% of cases thoracic exploration was necessary to establish the diagnosis.

Thoracotomy was performed in 723 cases and resection in 469 (32%); the latter operation was palliative in 73% of cases, the growth having extended beyond the lung. The operative mortality was 19%. Of the total number of patients subjected to resection, 47% were alive after 6 months, 33% after one year, 20% after 2 years, and 13·5% after 5 years. One patient who had a preoperative recurrent laryngeal nerve paralysis was alive and well 7 years later. It is suggested that if these results are to be improved upon, chest radiographs should be taken every 6 months in all men over 40 who have been heavy smokers. *R. L. Hurt*

1298. **Systematic Malignant Pulmonary Adenomatosis.** (Adenomatosi maligna sistematica dei polmoni)
E. Fasano and E. Miceli. *Rivista di patologia e clinica della tubercolosi* [*Riv. Patol. Clin. Tuberc.*] **27**, 257–285, Sept.–Oct., 1954. 23 figs., bibliography.

The authors describe in great detail the clinical and pathological features of a case of "systematic malignant pulmonary adenomatosis" in a man of 54 who died after one year's illness. This rare disease was first described by Dungal in 1938 and has been given various names, including "muco-epithelial hyperplasia of the lung" and "human jaagziekte", the latter expressing the resemblance of the condition to a virus disease occurring in sheep. The present authors, however, conclude that the disease is a form of alveolar-cell carcinoma. Many good radiographs and photomicrographs are reproduced, the world literature is fully discussed, and a bibliography is added. *L. Michaelis*

1299. **Tetracycline Therapy of Pneumococcal Pneumonia**
A. J. Palazzolo, G. M. Eisenberg, E. L. Foltz, M. Sones, and H. F. Flippin. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **4**, 1075–1081, Oct., 1954. 1 fig., 10 refs.

At Philadelphia General Hospital 70 patients suffering from primary pneumonia were treated with tetracycline. Their ages ranged from 14 to 84 years, 15 (21%) being 60 or over. Cases complicated by some types of cardiac disease, neoplasm, pulmonary fibrosis, tuberculosis, subacute bacterial endocarditis, and certain other conditions were excluded, but the series included 11 patients with cardiac disease, 6 with diabetes, and 4 suffering from alcoholism. Pneumococci were grown from 90% of the samples of sputum tested. The response to treatment, in promptitude of defervescence and the low incidence of secondary rises in temperature, compared favourably with the results obtained with penicillin in a similar series, 55 (78·5%) of the patients remaining afebrile after 48 hours' treatment. Radiological resolution was complete within 4 weeks in 43 cases.

The dose of tetracycline was 0·5 g. every 6 hours, and administration was continued for at least 7 days except to those patients who failed to respond, in which case other treatment was substituted. Toxic symptoms occurred in 4 cases (5·8%) but were mild, consisting in diarrhoea (2 cases), vomiting (1), and sore throat (1). There was one therapeutic failure, and 2 patients died, death in one case being the result of a cerebral vascular accident. The serum content of tetracycline was determined at intervals and showed a steady rise, reaching 4 μg. per ml. at the end of 48 hours. Occasional samples from some of the patients during continuous treatment contained the following concentrations: "early", 2 μg. per ml.; at 3 to 7 days, 5·5 μg. per ml.; at 8 days or more, 10 μg. per ml.

The authors conclude that tetracycline is suitable for the treatment of patients suffering from pneumococcal pneumonia who are sensitive to penicillin, and also in cases in which the aetiology is unknown but where there is reason to suspect that a Gram-negative organism is responsible.

[The authors may well be right in their conclusions, and it may be sound clinical practice under certain circumstances to act on their recommendations; but they adduce no evidence in support of the use of tetracycline in the treatment of infections by Gram-negative organisms or those "of unknown aetiology". No mention is made of any attempt to culture an organism in the cases that reacted with sore throat and diarrhoea.]
Bernard Freedman

1300. **Pulmonary Echinococcus. Surgical Treatment in 124 Hydatid Cysts**
J. A. Taiana, E. Schieppati, and V. Aracama Zorraquin. *Diseases of the Chest* [*Dis. Chest*] **26**, 686–692, Dec., 1954.

The authors briefly discuss the diagnosis and surgical treatment of pulmonary hydatid disease. At the Institute of Thoracic Surgery, Buenos Aires, they have operated on 104 patients with pulmonary hydatid cysts (a total of 124 cysts). Altogether 117 operations were performed, including resection in 59 cases of uninfected cyst and marsupialization in 39 cases of infected cyst. The importance of recognizing the presence of pneumonitis and bronchiectasis adjacent to the hydatid cyst is stressed. *R. L. Hurt*

1301. **Staphylococcal Pneumonia Occurring during an Influenza Epidemic**
R. B. Lefroy and D. D. Keall. *Australasian Annals of Medicine* [*Aust. Ann. Med.*] **3**, 299–304, Nov., 1954. 1 fig., 11 refs.

1302. **The Variability of Ventilatory Function in Emphysema**
J. Friend. *Clinical Science* [*Clin. Sci.*] **13**, 491–495, Nov., 1954. 6 refs.

Otorhinolaryngology

1303. **Difference Limen and Recruitment**
I. J. HIRSH, T. PALVA, and A. GOODMAN. *Archives of Otolaryngology* [*Arch. Otolaryng.* (*Chicago*)] **60**, 525–540, Nov., 1954. 4 figs., 32 refs.

The presence of recruitment, or an abnormally rapid increase in loudness sensation with increase of sound intensity, is now generally accepted as proof of the presence of a non-conductive hearing loss. It has further been suggested by Dix *et al.* (*Proc. roy. Soc. Med.*, 1948, **41**, 516; *Abstracts of World Surgery*, 1949, **5**, 102), though not universally accepted, that it is proof of a cochlear lesion and that recruitment is absent in retrocochlear lesions. Many methods of detecting recruitment have been developed, and the present authors here examine and criticize those which depend on measurement of the " difference limen " (D.L.) or the smallest recognizable difference in intensity between two tones. Such methods are based on two questionable assumptions: (1) that as the D.L. normally decreases as the intensity at which it is measured rises, in the recruiting patient the D.L. will always be less than in the normal subject, since in the former greater loudness is associated with the same intensity (loudness in relation to the D.L. being here regarded as more significant than intensity); and (2) that since the change in loudness corresponding to a given change in intensity is greater in the recruiting patient, his sensitivity to change in intensity will be greater and the D.L. smaller than normal.

They then examine a number of methods of testing for recruitment which are based on this principle. In Bekesy's method the points at which a tone of continuously increasing intensity is just heard and one of continuously decreasing intensity is just not heard are determined, but the authors do not accept this as measurement of the D.L. at threshold. In the method of Luscher and Zwislocki a tone is alternated between two intensity levels by an amplitude modulator, and it is claimed that whereas normally the D.L. lies between 10 and 16% pressure modulation, with partial recruitment it lies between 6 and 8% and with complete recruitment it is below 6%. The method of Denes and Naunton is to alternate two tones of different intensity, reducing the difference until the observer reports them equal or increasing it until they are reported different. With neither of these methods, however, have consistent results been obtained by other workers and they are therefore rejected as unreliable.

The authors have carried out tests for recruitment based on the measurement of speech discrimination, loudness balance, and D.L. on 18 normal subjects and 44 patients and found that whereas the results of the first method were confirmed by those of the second, the results of the D.L. tests were inconstant; nor could they confirm the finding of Denes and Naunton that the D.L. behaved differently in recruiting and non-recruiting cases. They conclude that although there may be some relation between the size of the D.L. and the presence of recruitment, the nature of this relation depends so much on the technique used that no one method of determining the D.L. can yet be recommended for general use. They regard the speech-discrimination test as reliable and point out that the difficulties of carrying out Fowler's and Reger's loudness-balance techniques have been exaggerated. *F. W. Watkyn-Thomas*

1304. **Are the Membranous Walls of the Endolymphatic Labyrinth Permeable?** [In English]
J. LEMPERT, E. G. WEVER, and M. LAWRENCE. *Acta oto-laryngologica* [*Acta oto-laryng.* (*Stockh.*)] Suppl. 116, 182–188, 1954. 5 figs., 2 refs.

In 1951 Meyer (*Z. Laryng. Rhinol. Otol.*, **30**, 455) described a series of observations suggesting that the membranous wall of the labyrinth is permeable to normal saline, basing his conclusions partly on the appearance of the labyrinth at operation, and partly on experimental work on animals.

The present authors have repeated his work and were able to show that the apparent collapse of the membranous canal during operation was an optical illusion, depending on the fact that fluid refracts the light rays so that an object immersed in fluid, when viewed obliquely, appears to be closer than it really is. In experimental work on the pigeon, they removed part of the membranous canal, having closed it first by tying a hair round both ends. The part removed was then floated in saline and was shown to keep its shape, and to collapse only when pricked with a needle. Meyer's conclusion that the membranous wall is permeable to normal saline is thus disproved. *William McKenzie*

1305. **The Effect of Various Operations on Hearing in Chronically Discharging Ears.** [In English]
T. PALVA and U. SIIRALA. *Acta oto-laryngologica* [*Acta oto-laryng.* (*Stockh.*)] Suppl. 116, 241–258, 1954. 1 fig. 37 refs.

In this discussion of the treatment of otitis and the resultant effect on hearing the authors, writing from the University Ear, Nose, and Throat Clinic, Turku, Finland, suggest that a simple mastoid operation should be considered if the discharge in cases of acute otitis persists for more than 3 weeks in spite of the administration of antibiotics. In chronic otorrhoea, no mastoid operation can improve the hearing if the perforation is in the pars tensa, but a modified radical mastoidectomy should be performed for perforations of the attic. If the hearing loss lies between 20 and 40 db., the incus and head of malleus may be removed without harm to the hearing. A loss of over 40 db. usually suggests involvement of the internal ear, and in this case the radical mastoid operation should be considered. But even the best results of a modified radical mastoidectomy show a loss of 25 to 30 db. because of interference with the ossicles.
William McKenzie

Urogenital System

1306. **The Action of Thiosemicarbazone on Renal Oedema in Children.** (Action de la thiosémicarbazone sur les néphropathies œdémateuses de l'enfance)
N. NEIMANN, M. PIERSON, and G. LASCOMBES. *Archives françaises de pédiatrie* [*Arch. franç. Pédiat.*] **11**, 943–950, 1954. 5 figs., 6 refs.

Reports in the German literature have suggested that the tuberculostatic thiosemicarbazones also exert a hypotensive and diuretic effect and that they help in the restoration of the serum protein pattern to normal. On the theory that these properties might all be useful in the treatment of nephritis with oedema in children, the authors treated 4 such cases at the Children's Hospital, Nancy, with 25 to 50 mg. of thiosemicarbazone daily for 10 to 20 days. In all 4 a considerable diuresis resulted, with loss of weight and the disappearance of oedema, but the albuminuria and the disturbance of the serum protein pattern were little influenced. No toxic effects were observed.

It is stated that the thiosemicarbazones are comparable in diuretic effect with ACTH or cortisone, have no undesirable side-effects, and can be given in the presence of hypertension.

[There were no controls and the onset of diuresis during thiosemicarbazone treatment in these 4 cases may have been purely coincidental. Nevertheless, the potential value of these drugs should be further investigated.]

John Lorber

1307. **The Venous Junction of the Glomerular Artery**
A. TRABUCCO and F. MÁRQUEZ. *Journal of Urology* [*J. Urol. (Baltimore)*] **72**, 1061–1073, Dec., 1954. 12 figs., 11 refs.

1308. **The Nephrotic Syndrome Associated with Thrombosis of the Renal Veins**
J. D. BLAINEY, J. HARDWICKE, and A. G. W. WHITFIELD. *Lancet* [*Lancet*] **2**, 1208–1211, Dec. 11, 1954. 4 figs., 13 refs.

The authors believe that in some cases the nephrotic syndrome may be caused by interference with the venous return from the kidney, and in support of this describe, from the Queen Elizabeth Hospital, Birmingham, the cases of 2 patients with ascending thrombosis of the inferior vena cava who developed the nephrotic syndrome. Necropsy in one case proved the presence of thrombotic occlusion of the two renal veins, and of many microscopic organized thrombi in the arcuate and interlobular veins. The glomerular tufts were unaffected, but patchy hyaline fibrosis was present in some glomeruli and others showed thickening of the capillary basement membrane. In the other case, from the clinical findings, a similar pathological process appeared highly probable, but as necropsy was refused it could not be confirmed. In neither of these two patients was there any evidence of past or present nephritics.

The authors also describe a third patient suffering from long-standing cardiac failure due to constrictive pericarditis who had developed the nephrotic syndrome. Within 3 months after pericardectomy had been performed the nephrotic symptoms were much less, and after a further period of 3 months there was no evidence of a return of the oedema or proteinuria.

L. H. Worth

1309. **Effects of Infusion of Hyperoncotic Dextran in Children with the Nephrotic Syndrome**
J. JAMES, G. GORDILLO, and J. METCOFF. *Journal of Clinical Investigation* [*J. clin. Invest.*] **33**, 1346–1357, Oct., 1954. 2 figs., 33 refs.

The diuretic effect of hyperoncotic (12%) infusions of dextran (average molecular weight 70,000) on 16 children with the nephrotic syndrome but free from evidence of renal failure was studied at the Children's Medical Center, Boston, in order to determine not only the clinical value of the treatment but also: (1) the effect of increased plasma volume on glomerular filtration rate; (2) the relation of plasma volume, serum albumin concentration, and glomerular filtration rate to the glomerular permeability to albumin; (3) the effect of increased post-glomerular colloid osmotic pressure on tubular reabsorption of water and solutes; and (4) the nature of the dextran-induced diuresis.

The intravenous administration of 3 to 8 infusions, each of 300 to 400 ml. per sq. metre body surface area, resulted in considerable loss of weight in 9 of the children, sometimes equalling the total estimated excess weight; the lowest body weight was usually noted 24 to 48 hours after the last infusion. Untoward effects included epistaxis, transient headaches, nausea, and abdominal pain. The final therapeutic advantage, however, was very slight, the longest period of freedom from oedema following therapy being one month. The infusion of dextran produced a marked increase in plasma volume, which was associated with a rise in renal plasma flow; this did not result in increased glomerular filtration rate in some cases, in which diuresis produced by dextran was certainly a tubular function. In discussion it is suggested that increased colloid osmotic pressure in the post-glomerular blood flow may reduce intrarenal peritubular oedema. The calculated permeability of the glomerular membranes to albumin was shown to be relatively increased during dextran transfusion and appeared to be independent of that for water. The exact mechanism of water diuresis after dextran infusion is not yet fully understood.

L. H. Worth

1310. **The Destructive Form of Pyelonephritis.** [In English]
S. G. JOKIPII. *Annales medicinae internae Fenniae* [*Ann. Med. intern. Fenn.*] **43**, 249–255, 1954. 5 figs.

Endocrinology

PARATHYROID GLANDS

1311. **A Study of the Phosphaturia Provoked by the Infusion of Calcium Salts; a New Test of Parathyroid Function** (Étude de la phosphaturie provoquée après perfusion calcique, nouvelle épreuve fonctionnelle parathyroïdienne)

L. JUSTIN-BESANÇON, H. P. KLOTZ, P. BARBIER, D. CLÉMENT, and —. PERROT. *Annales d'endocrinologie* [*Ann. Endocr. (Paris)*] **15**, 405–424, 1954. 5 figs., 14 refs.

A new test of parathyroid function devised by the authors at the Hôpital Broussais, Paris, is described; this is based on the inhibition of parathyroid secretion in the presence of hypercalcaemia induced by the infusion of calcium chloride solution. The decay of parathyroid hormone circulating in the blood is estimated to be complete in 3 to 5 hours, during which time urinary phosphate excretion should fall steadily, since it is normally dependent on the amount of hormone present. Theoretically, therefore, in hypoparathyroidism the excretion of phosphate should be unaffected by the induction of hypercalcaemia. The dose of calcium given was 1 mEq. per kg. body weight, given intravenously over a period of 3 hours. Phosphate and creatinine excretion were measured, by means of catheter specimens of urine, at hourly intervals, as also was the serum calcium level. In 6 normal subjects there was a progressive fall in phosphate excretion during the 3 hours. In 5 subjects with hypoparathyroidism following thyroidectomy and 6 with idiopathic hypoparathyroidism the fall in phosphate excretion was absent and there was even a considerable rise in phosphate output in some cases.

In 6 cases of spasmophilia and 10 of endocrine cataract the response was variable, a fall in phosphate excretion occurring in some cases and an increase comparable to that observed in hypoparathyroid subjects in others.

C. L. Cope

1312. **Idiopathic Hypoparathyroidism. A Study of Three Cases**

P. K. ROBINSON, E. A. CARMICHAEL, and J. N. CUMINGS. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **23**, 383–402, Oct., 1954. 4 figs., bibliography.

Details are given of 3 cases of idiopathic hypoparathyroidism seen at the National Hospital, Queen Square, London. The patients were observed for a period of 3 months, during which time calcium and phosphorus balance studies were carried out and the clinical response to administration of parathyroid hormone and dihydrotachysterol was noted.

The most striking finding was the response to the Ellsworth–Howard test, when a dose of 30 *B.P.* units of parathyroid hormone, the customary dose for this test, produced very little increase in the urinary excretion of phosphate. However, with much larger doses (5 to 10 times the amount) there was an increase in the serum calcium level and a decrease in the serum phosphate level. In the authors' view too much reliance should not be placed upon the results of this test; moreover it may not be possible strictly to distinguish idiopathic hypoparathyroidism from so-called pseudo-hypoparathyroidism. They suggest that there may be variations between the different preparations of parathyroid hormone.

The results obtained with dihydrotachysterol confirmed those of Albright *et al.*, who first showed that this substance caused a marked increase in urinary excretion of phosphate and an increase in the serum calcium level; the latter, however, was less than that achieved with calciferol.

G. A. Smart

THYROID GLAND

1313. **The Relationship of Thyrotoxicosis and Carcinoma of the Thyroid to Endemic Goitre**

F. W. CLEMENTS. *Medical Journal of Australia* [*Med. J. Aust.*] **2**, 894–897, Dec. 4, 1954. 2 figs., 7 refs.

In an attempt to determine whether endemic goitre causes any predisposition to thyrotoxicosis the mortality from the latter disease over the period 1911–50 in the various States of Australia, in which the incidence of the former differs widely, was studied with reference to sex and age. Mortality from thyrotoxicosis among males of all ages increased from about 2 per million in 1911–20 to a maximum of 6·9 per million in 1936–40; thereafter the rate fell to 3·3 per million in 1946–50. Mortality among females increased from about 25 per million in 1911–20 to a maximum of 42·2 per million in 1936–40 and then fell to 15·9 per million in 1946–50. The most dramatic fall in mortality after 1940 occurred in New South Wales, Victoria, and Western Australia. In Australia as a whole since 1926 the age group showing maximum mortality from thyrotoxicosis among females has changed from about age 45–59 to ages over 75. However, a cohort analysis suggests that the generation now forming the oldest age group has for some reason suffered high mortality throughout life from this cause.

The geographical differences in mortality during three periods, 1931–40, 1941–45, and 1946–50, for each sex were studied by comparing the number of observed deaths from thyrotoxicosis with those expected, after standardization for age, on the hypothesis that there was no difference in the mortality experience between States. In Tasmania and New South Wales, in both of which the incidence of endemic goitre is high, the observed deaths exceeded those expected in each period, the differences being significant at the conventional level ($P=0·05$) throughout for Tasmania, but only for females in the first two periods for New South Wales. Among the females of Victoria, South Australia, and Western

Australia, where endemic goitre is comparatively rare or absent, the observed deaths were less than expected, but significantly so only in the first period for each State and in the second for South and Western Australia. In general, therefore, a high incidence of endemic goitre appeared to be reflected in an increased mortality from thyrotoxicosis. A similar analysis of mortality from carcinoma of the thyroid during 1950–52 revealed no significant geographical differences, but the total number of deaths was small.

The suggestion is made that the recent decline in mortality from thyrotoxicosis is associated with a similar trend in the incidence of endemic goitre, which in turn may be attributed to an increasing tendency for persons living in the rural areas where endemic goitre prevails to obtain food from widely scattered sources of supply rather than exclusively from local sources as heretofore.

E. A. Cheeseman

1314. **Sudden Enlargement of Thyroid Gland**
P. MENOF. *Lancet* [*Lancet*] **2**, 996–999, Nov. 13, 1954. 22 refs.

At the General Hospital, Johannesburg, the unexpected observation of sudden enlargement of the thyroid gland during experimental infusion of noradrenaline directed the author's attention to possible antagonism between the adrenal glands and the thyroid gland. A review of the literature showed that transitory enlargement of the thyroid gland during infusion of noradrenaline or of adrenaline had been described by several authors, all of whom noted that interruption of the infusion was followed by flushing and a fall in blood pressure to below the pre-infusion level. This sudden enlargement of the thyroid gland has also been observed after paroxysms of hypertension in patients with adrenal tumours. The flushing and the low diastolic blood pressure point to a compensatory thyroid hypersecretion, which persists for a time after the excessive flow of noradrenaline into the body has ceased. This antagonism between the adrenal glands and the thyroid gland appears to find confirmation in cases of Graves's disease precipitated by a terrifying emotional experience (*Shreckbasedow*).

The sudden enlargement of the thyroid gland can be considered to be a response to overaction of the adrenal medulla and the outpouring of large amounts of noradrenaline. Thyroid secretion produces vasodilatation and lowers diastolic blood pressure, and is therefore antagonistic to noradrenaline, which raises the diastolic pressure and is a vasoconstrictor. There are several hypotheses to explain this vasodilator action of thyroid secretion. The author favours the theory of adrenaline–noradrenaline balance and antagonism. Thyroid overactivity, by neutralizing noradrenaline, would bring about a preponderance of the adrenaline effects—that is, vasodilatation (fall in diastolic pressure) and tachycardia.

On the basis of these observations the author considers that essential hypertension is due to an absolute or relative thyroid insufficiency and hence that administration of thyroid extract would benefit hypertensive patients. He claims to have obtained good results in 334 cases of hypertension treated with thyroid extract.

Richard de Alarcón

ADRENAL GLANDS

1315. **Life Maintaining Action of 9 Alpha Chlorohydrocortisone Acetate in Adrenalectomized Rats**
J. H. LEATHEM and R. C. WOLF. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol.* (*N.Y.*)] **86**, 724–725, Aug.–Sept., 1954. 4 refs.

In a study carried out at Rutgers University, New Brunswick, on adrenalectomized immature male rats all the animals survived for at least 20 days when given 15 μg. daily of chlorohydrocortisone acetate (CHCA), whereas ten times that amount of cortisone acetate was required to give the same protection. In similar animals 100% survival was also obtained with deoxycortone acetate in doses of 15 to 20 μg. A study of the gain in body weight showed that rats treated with cortisone acetate gained an average of only 13 g. in 20 days, whereas those maintained on CHCA gained an average of 56 g. To test the duration of action of the steroids, two groups of rats were given a single injection either of cortisone acetate (2·5 mg.) or of CHCA (0·25 mg.) immediately after adrenalectomy; a third group of untreated animals acted as a control. The control animals survived for 7 days, the cortisone-treated rats 10·5 days, and the CHCA-treated animals 18·5 days. A group given CHCA together with a protein-free diet survived only 12·2 days. A single injection of deoxycortone acetate had no effect on survival.

B. Nordin

1316. **Effect of Cortisone on Response to Endotoxin in Mature Rabbits**
L. THOMAS and R. T. SMITH. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol.* (*N.Y.*)] **86**, 810–813, Aug.–Sept., 1954. 11 refs.

The authors had previously observed in young rabbits that cortisone interfered with a protective mechanism, perhaps involving the reticuloendothelial system, against the vascular necrotizing action of injected endotoxin. In this further study carried out at the University of Minnesota Medical School, Minneapolis, 24 mature rabbits were given a daily injection of 10 mg. of cortisone per kg. body weight on 3 successive days; on the third day meningococcal endotoxin was injected intravenously and the effect compared with that of the same dose of endotoxin administered to 24 untreated controls. Of the latter, 18 died within 18 hours, but in none of these was there evidence of renal cortical necrosis, nor was there in any of the survivors which were killed at 24 hours. Although only 3 of the 24 cortisone-treated animals died, it was found nevertheless that 9 of this group showed renal cortical necrosis when killed and examined at 24 hours.

In a further study a group of 6 rabbits were given a single intramuscular injection of 10 mg. of cortisone 6 hours before the injection of meningococcal endotoxin. They all survived for 24 hours, and when killed were found to be free from renal cortical necrosis. Of 6 controls given the endotoxin but no cortisone, 3 died within 24 hours, but none developed renal lesions. In

another, similar, experiment it was found that cortisone prevented the early lethal reaction caused by small amounts of endotoxin following an injection of colloidal iron saccharate, but that it did not prevent the development of renal cortical necrosis. *B. Nordin*

1317. **Effects of Cortisone and Antibiotics on Lethal Action of Endotoxins in Mice**
P. GELLER, E. R. MERRILL, and E. JAWETZ. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **86**, 716–719, Aug.–Sept., 1954. 17 refs.

Working at the University of California School of Medicine, San Francisco, the authors have investigated the protective effects of cortisone in mice given lethal amounts of an endotoxin. A single dose of crude endotoxin of *Escherichia intermedium*, sufficient to cause death in 80 to 100% of animals within 48 hours, was injected intraperitoneally into mice. The administration of a single dose of 5 mg. of cortisone subcutaneously one hour before the endotoxin in some cases and simultaneously with it in others protected 60 to 90% of the animals from death, but failed to do so if injected one hour after the endotoxin. In view of reports of the reinforcing effect of some antibacterial drugs, chlortetracycline, penicillin, chloramphenicol, and streptomycin were administered in a wide range of doses, but only the last named, given in doses of 2 mg., gave any protection against the endotoxin, and that inconsistently. Furthermore, cortisone given one hour before and streptomycin given one hour after the endotoxin resulted in a higher mortality than occurred when cortisone alone was used to protect the animals. It was also shown that penicillin was equally if not more active in interfering with the protective effect of cortisone. *B. Nordin*

1318. **The Effects of Cortisone and Corticotrophin on the Human Adrenal Cortex**
H. B. STONER and H. J. WHITELEY. *Lancet* [*Lancet*] **2**, 992–994, Nov. 13, 1954. 14 refs.

The authors describe the anatomical and histochemical changes in the adrenal cortex of 4 adult patients who were receiving corticotrophin and of 3 who were receiving cortisone acetate at the time of death. The combined weight of the adrenal glands was determined after fixation in 10% formol–saline solution, and the width of the different zones of the cortex was measured in sections stained with haematoxylin and eosin. The physiological state of the cortex was assessed from the amount of sudanophilic and phenylhydrazine reacting material present and also from the number and size of birefringent crystals seen after treatment of the glands with digitonin.

The combined weight of the adrenal glands of the patients who had received corticotrophin was above the upper limit of normal, while the width of the zona fasciculata was about twice the normal, this accounting for the total thickening of the cortex. The surfaces of the glands were often nodular owing to cortical overgrowth. The diminution in the amount of sudanophilic and phenylhydrazine-reacting material present and the reduction in the size and number of the birefringent crystals revealed an increased secretory activity. These changes were patchily distributed in both the zona glomerulosa and the zona fasciculata, indicating that the zonation of the adrenal cortex is of anatomical rather than physiological significance.

The effects of cortisone therapy were the reverse of these. The adrenal glands weighed less than half the normal; this was due to cortical atrophy, since the medulla was unchanged. There was atrophy of the zona fasciculata, but it was difficult to determine the width of each zone because of the distortion of the cortical architecture. The amount of sudanophilic, phenylhydrazine-reacting, and digitonin-birefringent material present was greatly increased, indicating secretory inactivity.

These findings show that cortical damage can be caused by therapeutic doses of cortisone; the authors therefore suggest that corticotrophin should be given instead of cortisone whenever possible, since these changes may be irreversible. *Richard de Alarcón*

See also Tuberculosis, Abstract 1204.

DIABETES MELLITUS

1319. **Elevated Glucose Threshold in Kimmelstiel–Wilson Syndrome**
J. L. GRANT. *New England Journal of Medicine* [*New Engl. J. Med.*] **251**, 302–304, Aug. 19, 1954. 8 refs.

Finding that two patients with the Kimmelstiel–Wilson syndrome (intercapillary glomerulosclerosis) had a persistently high blood sugar level without glycosuria, the author examined the records of 11 cases in which the presence of intercapillary glomerulosclerosis had been proved at necropsy for evidence of a raised renal threshold for glucose in the results of glucose tolerance tests or, when these had not been carried out, from a comparison of records of the blood sugar level with those of the urinary sugar content. The average renal threshold for glucose in the 10 cases in which it could be determined was 225 mg. per 100 ml. *K. O. Black*

1320. **Femoral Neuropathy in Relation to Diabetes Mellitus. Report of 17 Cases**
J. I. GOODMAN. *Diabetes* [*Diabetes*] **3**, 266–273, July–Aug. [received Dec.], 1954. 6 refs.

In this report the author seeks to isolate neuritis of the femoral nerve as a distinct clinical entity which, in his experience, is the most frequently found lesion of the peripheral nerves in diabetes. Although commonly occurring as part of a multiple neuritis, certain symptoms and signs are characteristic of involvement of the femoral nerve trunk. Spontaneous pain over the anterior and lateral aspects of the thigh is common; the pain may then radiate beyond the area of distribution of the femoral nerve. In many patients pain can be produced on stretching the femoral nerve by means of the reversed Lasègue's test, weakness of the extensors of the knee (occasionally with wasting) may be found, and the

patellar reflex is often lost. Paraesthesiae over the distribution of the femoral nerve may be a prominent symptom, but objective sensory loss is not common. Of the 17 cases described by the author, 16 had diabetes mellitus and in 13 of these the diabetes was considered to be inadequately controlled.

The author appears to have tried most of the forms of treatment advocated for this disease, but in common with most observers finds that the only hope of relieving the condition is by strict stabilization of the diabetic state. When this has been achieved, pain disappears rapidly and other symptoms subside within about 3 months. *J. N. Harris-Jones*

1321. **Response of Diabetic Coma to Various Insulin Dosages**

K. SMITH and H. E. MARTIN. *Diabetes* [*Diabetes*] 3, 287–295, July–Aug., 1954. 5 figs., 4 refs.

Because of the wide variations in opinion concerning the treatment of diabetic coma the authors, working at the Los Angeles County Hospital (University of Southern California Medical School) have attempted to assess the effect of various insulin dosages on 43 patients who were in coma according to the criteria adopted (clinical state of ketosis accompanied by an alkali reserve of less than 9·1 mEq. per litre). The patients were divided at random into three groups, the numbers in which were 12, 18, and 13 respectively. The initial dose of insulin in Group 1 was 80 units, in Group 2 160 units, and in Group 3 240 units. Insulin administration was then continued at 2-hourly intervals in reduced dosage determined according to the blood sugar level, which was estimated before each dose. All groups were treated similarly in other respects, and each patient received about 2 litres each of normal saline and M/6 sodium lactate solution. Glucose was withheld until the blood sugar level fell to 300 mg. per 100 ml. On admission the average blood sugar levels in the three groups were 688 mg., 755 mg., and 820 mg. per 100 ml. respectively.

The end-point of coma was judged to have been reached when (1) there was clinical termination of coma, (2) the blood sugar level fell below 300 mg. per 100 ml., (3) the alkali reserve rose above 20 mEq. per litre, or (4) death ensued, whichever occurred first. The average time taken to reach this end-point in Group 1 was 9·2 hours; in Group 2,8·8 hours, and in Group 3,7·7 hours. These differences are not statistically significant. It was similarly shown that there was no significant difference between the three groups in the time taken for the blood sugar level to fall below 300 mg. per 100 ml. or for the alkali reserve to rise above 20 mEq. per litre. The surprisingly high mortality of 26% (11 deaths) was recorded, but only 3 of the deaths were considered to be directly due to diabetic coma, 2 of them being attributed to hypokalaemia.

[The authors do not state their criteria for the " clinical termination " of coma. In one of the fatal cases the patient was considered to have died of hypokalaemia although the serum potassium level before death was 7 mEq. per litre.] *J. N. Harris-Jones*

1322. **An Approach to the Prediction of Diabetes Mellitus by Modification of the Glucose Tolerance Test with Cortisone**

S. S. FAJANS and J. W. CONN. *Diabetes* [*Diabetes*] 3, 296–304, July–Aug., 1954. 6 figs., 13 refs.

Present methods of assessing carbohydrate tolerance may not be sufficiently sensitive to reveal the prediabetic state which is not infrequently present in the apparently healthy relatives of persons with diabetes. The authors, working at the University of Michigan Medical School, Ann Arbor, have therefore devised a modification of the glucose tolerance test in which cortisone is used to unmask any latent diabetic tendency. After a preliminary investigation to determine the dose of cortisone which was large enough to reveal any impairment of carbohydrate tolerance already present without impairing the tolerance of a healthy control subject, a trial was carried out on (1) 50 healthy subjects who had no recent family history of diabetes, and (2) 152 apparently healthy relatives of diabetic patients. The two groups were comparable in respect of age and sex distribution. Each subject was given a standard diet containing 300 g. of carbohydrate for 3 days and a standard glucose tolerance test was then carried out on two successive days, 50 mg. of cortisone being given by mouth 8½ and again 2½ hours before the second test. (Heavier patients were given 62·5 mg. of cortisone at the same time intervals.)

A diabetic curve was obtained in the initial standard test in one member of Group 1 and in 29 (19%) of Group 2. Of the 37 members of Group 1 on whom the cortisone–glucose tolerance test was performed, the result was negative in 36, a diabetic curve being obtained from one subject who had given a normal curve in the standard test. Of the 123 members of Group 2 who had given a normal curve in the standard test, the cortisone test was performed on 75, of whom 18 (24%) gave a positive response in that the curve was clearly of the diabetic type. In 3 of those classed as diabetic on the evidence of a borderline curve in the standard test the cortisone–glucose tolerance test produced an obvious diabetic curve. Similarly in 6 obese patients whose standard curve was initially diabetic but had become normal after weight reduction the cortisone–glucose tolerance test produced again a classic diabetic curve.

The authors therefore conclude that in screening the apparently healthy relatives of diabetic patients three groups may emerge, the first (19%) giving an obvious diabetic curve with the standard glucose tolerance test, the second (24%) showing impaired carbohydrate tolerance only with the cortisone–glucose tolerance test, and the third giving no evidence of impaired carbohydrate tolerance in either test.

[This is an excellent study, and readers are advised to consult the original for details. The only point over which disagreement might arise is the old problem of what constitutes a normal glucose tolerance curve.]

J. N. Harris-Jones

See also Pathology, Abstract 1131; and Tuberculosis, Abstract 1203.

The Rheumatic Diseases

1323. **Some Variations in the Clinical Course of the So-called Non-specific Infectious Arthritis.** (Некоторые варианты клинического течения так называемого неспецифического инфекционного артрита)
I. I. MAKARENKO. *Советская Медицина* [*Sovetsk. Med.*] 20–24, No. 10, Oct., 1954.

The symptoms of so-called non-specific infectious arthritis are very numerous. Running parallel to the affection of the joints there are definite changes in the endocrine system; 2 of the author's patients had hyperthyroidosis and hypofunction of the ovaries. Changes also occur in the lymphatic system and the author states that a generalized enlargement of the lymph nodes may sometimes be mistaken for a lymphogranuloma; one patient had an affection of the urinary system similar to an amyloid nephrosis. There are also changes in the cardiovascular system manifested by arterial hypotension, or by dilatation of the capillaries of the palms of the hands producing an appearance resembling the condition called " liver palms ". One patient had a haemorrhagic vasculitis. All the author's patients suffered from excessive sweating and tachycardia.

It is considered most significant that all the patients did not respond to the therapeutic action of the antibiotics and that in a certain number improvement occurred only when cortisone and ACTH were given.

H. W. Swann

1324. **The Development and Nature of Osteoarthritis of the Hip Joint**
K. H. PRIDIE. *Rheumatism* [*Rheumatism*] **11**, 2–7, Jan., 1955. 9 figs.

1325. **Cheilotomy and Multiple Perforations in the Treatment of Osteoarthritis.** (Cheilotomie e perforazioni multiple nella cura della artrosi deformante)
M. BARBIERI. *Minerva chirurgica* [*Minerva chir. (Torino)*] 9, 981–996, Nov. 15, 1954. 34 figs., 31 refs.

The treatment of 12 patients with stiff and painful joints by cheilotomy combined with multiple drilling of the joint surface is reported from the Orthopaedic Clinic of the University of Genoa. In 6 cases the knee was affected, the joints involved in the remaining cases being the elbow, hip, and ankle. The author reviews the results in this small series (the follow-up period being 1 to 4 years in 7 of the 12 cases) and claims that in 90% the results were good, although in no case were all the essential features of the condition—pain, limitation of movement, and instability—eliminated, while in some of the cases these symptoms were aggravated by the operation.

[The arthritic changes shown in the radiographs reproduced are not of comparable origin or nature, nor do the photographic illustrations permit the reader to judge for himself whether or not there has been an increase in the range of movement. The claims made for this method in the treatment of osteoarthritis are not admissible on the evidence provided by a small series of heterogeneous cases, nor are they borne out by the follow-up details given.] *L. Michaelis*

RHEUMATIC FEVER

1326. **The Diagnostic and Therapeutic Aspects of Rheumatic Activity** (Les aspects diagnostiques et les aspects thérapeutiques de l'activité rhumatismale)
R. RAYNAUD, J. ROBERT D'ESHOUGUES, P. MINICONI, M. FERRAND, P. PASQUET, and V. PASQUET. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **30**, 4051–4060, Nov. 20, 1954. 2 figs.

The disease process of rheumatic fever may be active in the absence of any clinical manifestation. After subsidence of an acute episode, it may continue quietly for months or even years, during which time irreversible changes in the heart are established. From the authors' detailed study of 50 cases of rheumatic fever the most interesting conclusion emerges that changes in the level of serum mucopolysaccharides (glucoproteins), revealed by paper electrophoresis, provide the most reliable criterion of this activity. After migration of the serum glucoproteins under electrophoresis, the paper bands are treated with a staining reagent which marks their distribution and extent and clearly reveals any change from the normal. The result is referred to as a " glucidogram ".

All 50 patients studied showed some sign of activity; in 41 cases there was an acute attack, in 4 there was active rheumatic carditis, and 5 were cases of well-compensated valvular disease showing either an increased P–R interval in the electrocardiogram, or an increase in erythrocyte sedimentation rate, or both. In all these cases without exception the glucidogram showed an important increase in the α_1 and α_2 glucoprotein fractions. Thus the surface on the glucidogram occupied by the α_1 fraction was increased up to 200 sq. mm. (normal 50 to 100 sq. mm.) and that corresponding to α_2 was 400 sq. mm. instead of the normal 150 to 200 sq. mm. This was the one constant feature of all the authors' cases, and although the degree of increase in the α_1 and α_2 glucoprotein fractions did not run parallel with the clinical severity, the authors believe that it is an expression of the potential activity of the disease, and therefore of the greatest prognostic value.

In 32 cases repeated electrophoretic tests were made during treatment, which in 20 cases consisted in administration of cortisone, in 11 of sodium salicylate, and in one of aspirin only. Cortisone treatment was continued for 6 weeks in progressively decreasing doses from 300 mg. daily in the first few days to 100 mg.

during the 4th, 5th, and 6th weeks, being followed by aspirin in doses of 4 to 6 g. daily for 3 to 6 months. Of the 11 patients treated with sodium salicylate, 9 received 6 g. daily for 3 weeks, the drug being given intravenously in a solution containing glucose; this was followed by oral administration of sodium gentisate, 10 g. daily, for several weeks. The remaining 2 patients received salicylates both intravenously and orally. The clinical response was almost identical in these two treatment groups. In 13 cases the glucidogram became normal in less than 4 weeks, in 7 cases the period required was from 5 to 7 weeks, while in a further 7 the serum disturbance persisted beyond the 7th week (5 cases could not be followed up). These results are considered to be consistent with the general impression of the evolution of untreated rheumatic fever.

Their observations lead the authors to three main conclusions. (1) Neither sodium salicylate (or aspirin) nor cortisone has any action on the activity of the rheumatic process itself. (2) The glucidogram is the only reliable criterion of this activity, and by means of it treatment should be controlled; this is especially important in cases treated with cortisone, since the hormone affects the erythrocyte sedimentation rate and thus destroys its value as a criterion of activity. (3) In all attacks of rheumatic fever therapeutic measures should continue as long as the glucidogram remains abnormal, even though the clinical signs, the electrocardiographic findings, or any other laboratory test may seem to suggest that they could be stopped. *Kenneth Stone*

1327. **Rheumatic Fever and Rheumatic Heart Disease in Children as Seen in Clinic Practice. I. Clinic Diagnostic Technique**

L. L. Davis and M. H. Greene. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **88**, 427–438, Oct., 1954. 32 refs.

The authors of this paper describe the work of the diagnostic rheumatic fever clinic at Meadowbrook Hospital, Long Island, New York, to which 306 children were referred by their family doctor during the school year 1951–2 for "evaluation of puzzling cardiac findings or questionable rheumatic symptomatology". The classic form of rheumatic fever is now less common than it used to be, and the "typical" case, in the authors' experience, is the child with a smouldering carditis and few, if any, of the orthodox signs of rheumatism, presenting a formidable problem in diagnosis.

Great importance is attached at this clinic to the standardization of procedure in examination and in the recording of the results—the methods used are described in detail—and an attempt has been made to classify the findings which have proved most important and useful for the diagnosis of rheumatism in three categories, as follows.

1. *Positive evidence of rheumatic disease.* (*a*) Radiological signs of enlarged left atrium and left ventricle in the absence of congenital heart disease. (*b*) Systolic murmur of Grade 3 or greater intensity at the apex transmitted to the axilla. (*c*) Transient prolongation of A-V conduction in the presence of rheumatic symptoms indicates the presence of carditis. (*d*) Prolonged $Q–T_c$ similarly indicates the presence of carditis. (*e*) In the presence of cardiac findings of questionable significance, a history of rheumatic heart disease in both parents is considered to justify the diagnosis of "potential heart disease".

2. *Presumptive signs.* (*a*) Family history of rheumatic disease in a "sickly" child complaining mainly of abnormal fatiguability. (*b*) Changes in heart sounds or murmurs on repeated examination. (*c*) Choreiform movements or a history of chorea with minimal cardiac signs. (*d*) "Non-specific" electrocardiographic changes, such as notched P waves, in a child otherwise well. (*e*) A generally enlarged heart without alternative explanation.

3. *Helpful diagnostic characteristics.* (*a*) A report that the child is not well, though not definitely ill. (*b*) Marked depletion of vital capacity in an older child without respiratory disease. (*c*) Progressive pallor without a corresponding degree of anaemia.

M. MacGregor

1328. **The Role of the Streptococcus in the Pathogenesis of Rheumatic Fever**

F. J. Catanzaro, C. A. Stetson, A. J. Morris, R. Chamovitz, C. H. Rammelkamp, B. L. Stolzer, and W. D. Perry. *American Journal of Medicine* [*Amer. J. Med.*] **17**, 749–756, Dec., 1954. 1 fig., 32 refs.

To determine the relative importance of the Group-A streptococcus in the pathogenesis of rheumatic fever a study was made of young airmen with exudative tonsillitis and pharyngitis admitted to hospital at a U.S. Air Force base in Wyoming. Included in the study were 420 men given 900,000 units of procaine penicillin in aluminium monostearate on the 9th, 11th, and 13th days after the onset of illness, 230 men given sulphadiazine, 2 g. on admission and 1 g. every 6 hours for 5 days, and 220 men who received a placebo and acted as controls. A total of 20 rheumatic episodes occurred between the 10th and 46th days among the sulphadiazine-treated men and the controls, compared with 3 episodes among the 420 men who received penicillin after the onset of the illness.

It was concluded that penicillin would prevent rheumatic fever if given 9 days after the onset of illness, but that sulphadiazine was ineffective. Such delay in giving penicillin led to the eradication of streptococci from the nasopharynx, but did not significantly affect the antistreptolysin response. The authors suggest that the development of rheumatic fever requires the presence of living streptococci throughout convalescence from a streptococcal infection.

[The authors' argument is weakened by the fact that 5 men who received penicillin on the 9th day had already developed rheumatic fever before the drug was given, and 3 controls and 2 sulphadiazine-treated subjects had also developed rheumatic fever before the 9th day. It may well be that such cases could be prevented by giving penicillin in the orthodox way—namely, at the beginning of an attack of Group-A streptococcal sore throat.]

R. S. Illingworth

Physical Medicine

1329. **The Use of Traction in Backache**
E. H. FRAZER. *Medical Journal of Australia* [*Med. J. Aust.*] **2**, 694–697, Oct. 30, 1954. 3 figs., 18 refs.

There are many causes of low backache, the most frequently encountered being physical and emotional trauma. The end-result of most lesions is muscle tension, and to counteract this spinal traction is valuable. A vertical traction appliance is described in which use is made of the patient's body weight, and the resistance due to friction when a traction table is used is avoided. It is claimed that almost every joint in the body may be stretched by this method. The appliance consists of a self-locking hoist fixed to a wall, the hoist being connected by a wire over a ceiling pulley to a steel cross-bar. A spring balance is incorporated in the traction wire. The patient is suspended from the cross-bar by a special, well-padded corset, which fits round the thorax. A leather gaiter fixed to each leg or a pelvic band is attached to a steel bar fastened to the floor. By this method traction up to 400 lb. (181 kg.) is given for about 5 minutes, the traction being applied gradually and increased at each session. The author claims good results in 80 to 90% of cases which failed to respond to other methods of treatment, and he quotes the results obtained with traction at various centres in Europe, the percentage of good results at 6 centres averaging 69·8. He advocates administration of sedatives, such as bromide, as a routine and mephenesin 10 minutes before traction is applied. All patients are examined clinically and radiologically before treatment is started, but care should be exercised in the use of this method on patients with peptic ulcer, hypertension, hernia, cardiac disturbances, or gross haemorrhoids. *J. B. Millard*

1330. **Clinical Uses of Chronaxie Determinations**
W. J. ERDMAN. *Archives of Physical Medicine and Rehabilitation* [*Arch. phys. Med.*] **35**, 638–642, Oct., 1954. 7 refs.

The author asserts that the information obtained from an estimation of the chronaxie of excitable tissue can be as valuable in the diagnosis and prognosis of lower motor neurone disease as that obtained by electromyography. He recalls the definition of the rheobase and the history of the elaboration of the concept of chronaxie, and claims that chronaxie can be estimated with less than 10% error if standardized techniques are used. Its estimation may be regarded as a refined method of testing for the reaction of degeneration. False positive results are never obtained, and an increase in chronaxie is positive proof of lower motor neurone damage.

The author gives a detailed description of his technique and a brief analysis of the findings in a series of 246 patients suffering from a variety of neuromuscular diseases. He found that in all those with lower motor neurone lesions the chronaxie was elevated, the normal value for muscle being about 0·1 millisecond and any value over 1 millisecond being regarded as abnormal. He claims that the estimation of chronaxie is convenient, accurate, and painless, and suggests that it should be used more frequently as an aid to diagnosis in conjunction with other electrical tests. *W. Tegner*

1331. **Rehabilitation of the Patient with Multiple Sclerosis**
M. MARKS and J. GOODGOLD. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **156**, 755–757, Oct. 23, 1954. 19 refs.

The results of treatment of disseminated sclerosis are difficult to assess because the natural course of the disease is unpredictable, but the present authors attempt critically to evaluate the results obtained at a rehabilitation centre in New York where, during the last 5 years, 200 patients have been seen. They do not advocate one specific treatment regimen for patients with disseminated sclerosis, but rather a plan of treatment suited to each individual's needs. This plan should be realistic in aim and should be reassessed if the disease becomes progressive; treatment should be discontinued if deterioration becomes apparent. The patient should be encouraged to undertake active exercise to the point of fatigue and beyond, but not to the point of exhaustion. There is no evidence, the authors state, that rehabilitation has any influence on the primary pathological process in disseminated sclerosis, but it does appear to be a factor in reducing the incidence and severity of secondary complications.

Treatment is directed primarily at functional improvement by exercise and at the performance by the patient of those activities of daily life " which are necessary for proficient function in his own environment ". Prostheses, self-help devices, and wheelchairs may be necessary. Drugs such as mephenesin have been found relatively ineffective in the control of spasticity. Before the patient attempts to walk balance exercises are essential, and even if walking is not possible, the standing position for 20 minutes each day will reduce secondary metabolic complications of inactivity. Progressive resistance exercises are helpful in strengthening weak muscles, but in view of the proneness of these patients to fatigue, the exercises should be carried out judiciously. Occupational therapy helps in muscle re-education and coordination and stimulates the patient's interest; it also serves for vocational training.

Drugs such as atropine, methantheline, caramiphen hydrochloride, and " bethanechol " chloride are of value in the control of bladder symptoms. If urinary incontinence persists the patient must be trained in the use of proper aids. Loss of bowel control must be overcome by retraining; in only one of the present series of cases was this unsuccessful. *J. B. Millard*

Neurology and Neurosurgery

1332. **The Use of Prolonged Interrupted Sleep in the Treatment of Neurological Diseases.** (Опыт применения длительного прерывистого сна в клинике нервных болезней)
V. A. Ershov. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **54**, 941–944, Nov., 1954.

The author reports, from Stalingrad, his experience with prolonged, interrupted sleep in the treatment of organic and functional nervous disorders. The treatment was carried out in isolated, darkened, sound-proof wards. In most cases sleep was induced with "barbamyl" in combination with chloral hydrate, barbitone, barbitone sodium, or phenobarbitone, these drugs being replaced by inactive substances for toxic patients. The latter slept from 14 to 20 hours a day for a period of 12 to 15 days. The results were very good in patients with chorea, and were also favourable in cases of neuritis, polyneuritis, disseminated sclerosis, and hypertension with neurological involvement. Evidence of deterioration during sleep therapy was observed only in cases of residual epidemic encephalitis. In discussion the author mentions also the good effect of sleep therapy in the treatment of psychoneurosis. *L. Crome*

1333. **The Absorption and Excretion of Radiocopper in Hepato-lenticular Degeneration (Wilson's Disease)**
W. B. Matthews. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **17**, 242–246, Nov., 1954. 3 figs., 19 refs.

In a study carried out at King's College Hospital, London, to determine whether the accumulation of copper in the body which is a feature of hepato-lenticular degeneration is due to over-absorption of the metal or to undue retention in the tissues, radioactive copper (^{64}Cu), was given orally as copper sulphate to 2 young men with the more chronic "pseudosclerotic" form of Wilson's disease. At the time of the test the first patient was almost symptom-free after repeated treatment with courses of BAL and continuous glycine by mouth, but the second was severely incapacitated; both showed the characteristic amino-aciduria and increased urinary excretion of copper. Three young men with unrelated chronic neurological disease and one normal subject acted as controls.

After a preliminary test 4·95 mg. (125 μc.) of ^{64}Cu was given; absorption curves showed a peak at one to 2 hours. Once the peak had been reached, every point on the curves was higher for the patients than for the controls at corresponding times. A larger proportion of the ingested dose of copper was recovered in the faeces of the controls than in those of the patients; on the other hand the patients passed a much larger proportion of the dose in the urine. This increased rate of urinary excretion was present even when the plasma copper level was almost identical with that of the controls, at the peak of the absorption curves, and continued after the peak had been passed.

In view of the small number of patients available the author is reluctant to draw definite conclusions, but suggests that these findings lend support to the view that over-absorption of copper occurs in patients with Wilson's disease and that the plasma contains copper which is bound in an abnormal form and which is thus able to pass through the glomerular filter.

Adrian V. Adams

1334. **A New Syndrome: Progressive Familial Infantile Cerebral Dysfunction Associated with an Unusual Urinary Substance**
J. H. Menkes, P. L. Hurst, and J. M. Craig. *Pediatrics* [*Pediatrics*] **14**, 462–467, Nov., 1954. 7 refs.

1335. **Paper Electrophoretic Studies in Multiple Sclerosis**
E. Roboz, W. C. Hess, F. M. Forster, and D. M. Temple. *Neurology* [*Neurology*] **4**, 811–817, Nov., 1954. 1 fig., 19 refs.

The blood proteins in 22 cases and the cerebrospinal fluid proteins in 10 cases of multiple sclerosis were studied by the technic of paper electrophoresis. In the blood serum study the cases were divided into two groups representing early and later stages of the disease. Only a trend of deterioration between the two groups could be established. No statistical significance could be attached to the differences. The decrease of albumin in the blood serum is considered to be nonspecific for multiple sclerosis, representing rather a general metabolic deterioration. The protein pattern of the cerebrospinal fluid is characterized by significant changes in gamma globulin. It is recommended that the protein pattern of the spinal fluid and not the blood serum should serve as a basis for diagnosis.—[Authors' summary.]

1336. **Studies in Myasthenia Gravis: Cardiac and Associated Pathology**
H. Mendelow and G. Genkins. *Journal of the Mount Sinai Hospital* [*J. Mt Sinai Hosp.*] **21**, 218–225, Nov.–Dec., 1954. 4 figs., 11 refs.

In the most serious cases of myasthenia gravis the muscles of respiration are often involved, but it has generally been assumed that the cardiac and smooth muscles are unaffected. In a study carried out at Mount Sinai Hospital, New York, on 10 consecutive fatal cases of myasthenia gravis, with or without thymoma, focal myocardial necrosis was demonstrated at necropsy in 9; it varied from scattered areas of atrophy, with vacuolization of myofibrils and slight lymphocytic infiltration, to severe and extensive myocardial necrosis with inflammatory reaction. The skeletal muscles were found to be involved in 7 cases, lymphorrhages being the only finding in 4, but focal necrosis with surrounding inflammatory

changes was present in the other 3. In 2 cases of malignant thymoma presenting as a mediastinal tumour lesions in the heart and skeletal muscle were found; in both these cases myasthenic symptoms developed after treatment of the tumour. It would appear, therefore, that there may be some relationship between thymoma and myocardial necrosis, for such necrosis occurred in 4 of the cases of myasthenia gravis associated with thymoma. It is suggested that post-mortem histopathological studies should be carried out on the heart muscle of all patients dying of myasthenia gravis, and that comparison of the cardiac lesions with the skeletal muscle lesions might reveal a common pathogenetic factor. *J. Foley*

1337. **Cheiralgia Paresthetica—Wartenberg's Disease**
B. E. SPROFKIN *Neurology* [*Neurology*] **4**, 857–862, Nov., 1954. 2 figs., 10 refs.

The author comments that except for the 5 cases of cheiralgia paraesthetica reported in 1932 by Wartenberg (who gave the condition its name), this syndrome of a mononeuropathy of the radial nerve has received scant attention, but that it may be less rare than has been supposed, since 3 cases have been seen at the Vanderbilt University School of Medicine, Nashville, Tennessee, in the last year. All 3 patients complained of painful sensations over the ulnar side of the thumb, and in 2 cases there was cutaneous discoloration over the painful area; in the third there was oedema and hyperaemia. No obvious aetiology could be demonstrated, and none of the patients was wearing a tight wrist-watch strap. All 3 made a complete spontaneous recovery within 2 weeks, no treatment beyond local rest of the hand being advised.

The author emphasizes that in view of the benign and ephemeral character of the disorder it is important not to embark on useless and perhaps hazardous diagnostic procedures. *N. S. Alcock*

DIAGNOSTIC METHODS

1338. **EEG Changes during Cinematographic Presentation. (Moving Picture Activation of the EEG)**
H. J. GASTAUT and J. BERT. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **6**, 433–444, Aug., 1954. 6 figs., 12 refs.

Working at the Marseilles Faculty of Medicine and using conventional recording techniques, the authors have investigated modifications occurring in the electroencephalogram (EEG) in 80 subjects, of whom 62 were psychiatrically normal, during the showing of certain cinematographic films. These films, consisting of excerpts from newsreels, were designated "control films", being judged to be "devoid of any image capable of inducing emotional reactions in most of the subjects".

Three significant modifications in the EEG are described and discussed. (1) In 17 subjects the experimental situation favoured the gradual appearance of a Rolandic *rythme en arceau*, except when the subject identified himself with one of the active figures on the screen. [It is not stated to which group these subjects belonged, nor whether a film in which the subject identified himself with one of the figures was still considered to be a "control film" for this subject.] The authors conclude that the progressive increase observed in the rhythm *en arceau* was probably dependent on a concomitant increase in muscular relaxation. (2) In 39 cases the frequency of occurrence of occipital sharp waves (lambda waves) was increased; this was considered not to be due to the rhythmic repetition of projected images (at a rate of 24 cycles per second), but to be "functionally related to very complex cerebral factors secondarily determined by visual perception". (3) The alpha rhythm, present when the subjects' eyes were open before the projection, was blocked in all cases for about 30 seconds at the beginning of the film, but reappeared to a varying extent in all but 20 cases, in which it remained almost completely blocked. Its reappearance is attributed to loss of attention.

These findings are compared with those of other workers, and it is claimed that the future use of "test films" will "greatly increase the value of movie activation". *W. A. Cobb*

1339. **Parietal Focal Theta Rhythm**
W. COBB and G. MULLER. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **6**, 455–460, Aug., 1954. 2 figs., 8 refs.

The electroencephalograms of 37 patients are described, in which the only, or major, abnormality was a sharply focal rhythm at 7 ± 2 c.p.s., in one or other parietal region; it was not much affected by eye-opening, startle, or over-breathing, and was usually readily distinguishable from the alpha rhythm, although the difference in frequency might be small.

All the patients had lesions in the parietal region, the majority being tumours. Some of these were in part superficial or cortical, but in all cases the roof of the body of the lateral ventricle was involved. It is suggested that partial isolation of an area of cortex is the essential factor in the production of focal theta rhythm; a possible identity with the *rythme en arceau* of Gastaut is discussed.

Parietal focal theta rhythm is a reliable guide to location. If such obvious causes as local cerebral trauma are excluded there is a one-in-three chance that the lesion is a meningioma.—[Authors' summary.]

1340. **The Electroencephalogram in Essential Hypertension and Chronic Cerebrovascular Disease**
J. A. ROBERTS and M. WALKER. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **6**, 461–468, Aug., 1954. 6 figs., 7 refs.

The occurrence of electroencephalographic abnormalities in 104 patients with essential hypertension or cerebral arteriosclerosis, or both, was studied at the Maida Vale Hospital for Nervous Diseases, London. The tracing was abnormal in 14 (52%) of the 27 patients with essential hypertension but without signs or symptoms of cerebral vascular disease, and in 37 (82%) of the 45 with hypertension and clinical evidence of cerebral

vascular disease but with no history of epilepsy. The tracing was abnormal in all of 24 cases in which hypertension was associated with epilepsy and in all of 8 cases in which there was evidence of cerebral arteriosclerosis without hypertension, in 4 of which there was a history of epilepsy. The abnormalities were various and quite unspecific. *W. A. Cobb*

1341. **Electroencephalographic Investigation of Patients with Sleep Disturbances in Reactive States.** (Электроэнцефалографическое исслеование больных с нарушениями сна при реактивных состояниях)
N. A. GAVRILOVA. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **54**, 915–918, Nov., 1954. 3 figs., 2 refs.

Working at the Psychiatric Research Institute of the Soviet Ministry of Health, Moscow, the author investigated electroencephalographically 26 patients suffering from different reactive states, but all of whom had in common the symptom of sleep disturbance. The records showed some tachyrhythmia but absence of significant dysrhythmia, sharp waves being rare. It is suggested that the sleep disturbances in such patients are probably produced by excitatory cortical phenomena preventing the even spread of inhibition over the cortex during sleep. *L. Crome*

1342. **Localization of Brain Lesions by Means of RISA**
J. G. RUSHTON, H. J. SVIEN, and E. J. BALDES. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **29**, 478–485, Aug. 25, 1954. 1 fig.

The authors have tested at the Mayo Clinic a method for the location of intracranial lesions in which the intravenous injection of a solution of radioactive iodine in human serum albumin (R.I.S.A.) is followed 20 to 30 hours later by measurement of the radioactivity on the surface of the head by means of a counter. For this a Texas tube was used, and the patients were prepared by giving 10 drops of Lugol's iodine solution 3 times during the previous 24 hours. The usual dose of R.I.S.A. was such as to contain 0·3 mc. of radioactive iodine. A preliminary study on a group of 37 patients without intracranial lesions showed that in the " normal " range of counts there was an error, inherent in the method, of 4 to 6%, and that differences in the counts as high as 10 to 12% were found in various regions of the cranium in the absence of any lesion. It was therefore considered that no differential counts of less than 14% should be regarded as a positive indication of intracranial lesion. Counts recorded during the first 20 hours following the injection were found to be unreliable, while after 30 hours all differences tended to disappear.

The subsequent investigation of 84 patients with known intracranial lesions showed that the procedure in its present stage of development is of little diagnostic value. For example, out of 38 vascular lesions only 4 were located, the site of 3 out of 6 meningiomata was correctly diagnosed, but only 5 out of 18 astrocytomata were located and in addition 2 false locations were obtained. Investigation of other types of tumour proved even less successful. *Donald McDonald*

CEREBRAL VASCULAR DISORDERS

1343. **Cerebral Vascular Disorders**
RUSSELL BRAIN. *Annals of Internal Medicine* [*Ann. intern. Med.*] **41**, 675–681, Oct., 1954. 4 figs.

In 1952 vascular disease of the nervous system was responsible for 14% of all deaths occurring in England and Wales. The author presents a series of 200 cases of such disease, 100 from the London Hospital and 100 from his private practice, and analyses them with special reference to the age distribution, the type of lesion, and the relation between the two. In the series as a whole about one-half of the patients were over 60 and about one-quarter below 50 years of age, but whereas 67% of the private patients were over 60, 63% of those admitted to hospital were below this age, reflecting the greater frequency of subarachnoid haemorrhage, requiring admission to hospital, among younger patients. Hypertension was present in 50% of all cases.

The author stresses the value of angiography in the diagnosis of cerebral vascular lesions, including angiomata and aneurysms, and particularly in elucidating the symptomatology of obstruction, due to atheroma or thrombosis, of the internal carotid artery. The effects of a complete block of the artery on one side are extremely variable, depending on the adequacy of the collateral circulation through the circle of Willis. There may be no symptoms at all or there may be massive infarction of the whole hemisphere, with hemiplegia, hemianaesthesia, and hemianopia. *G. S. Crockett*

1344. **Cerebral Vascular Diseases: Their Significance, Diagnosis and Present Treatment, Including the Selective Use of Anticoagulant Substances**
I. S. WRIGHT and E. MCDEVITT. *Annals of Internal Medicine* [*Ann. intern. Med.*] **41**, 682–698, Oct., 1954. 3 figs., 9 refs.

The authors quote statistics to emphasize the importance of cerebral vascular disease as a social problem, pointing out that in 1952 27% of the 170,000 persons dying in the U.S.A. from cerebral vascular accidents were of working age—between 25 and 65. It is estimated that where the blood pressure and cardiac rhythm are normal, thrombosis causes 60 to 85% of the deaths in this disease group, haemorrhage and embolism accounting for the rest. The differentiation of thromboembolic disorders from those due to haemorrhage is important from the point of view of treatment. Evidence of raised intracranial pressure—such as papilloedema and unequal pupils—and rapidly spreading neurological signs suggest haemorrhage. Lumbar puncture with measurement of the cerebrospinal-fluid (C.S.F.) pressure is considered to be a safe and valuable procedure. It must always be borne in mind, however, that the absence of blood from the C.S.F. does not completely rule out the possibility of haemorrhage.

The authors discuss the treatment of thromboembolism by the administration of carbon dioxide and by stellate ganglion block and conclude that the worth of these two procedures has not yet been proved. They

then outline, with illustrative case histories, their experience of the use of anticoagulants in cases of cerebral thrombo-embolism, claiming that such treatment reduces the frequency of cerebral embolic incidents in patients with rheumatic heart disease or acute myocardial infarction and lessens the risk of repeated thrombosis in those with cerebral vascular disease. [No detailed account of the treatment advocated is given, nor any indication when it should be started or stopped, the impression being given that these patients are to join the ever-growing army of those who must be given anticoagulants indefinitely.] *G. S. Crockett*

1345. **The Ocular Symptoms of Intracranial Aneurysm**
J. MacD. Holmes. *Transactions of the Ophthalmological Society of the United Kingdom* [*Trans. ophthal. Soc. U.K.*] **74**, 549–557, 1954. 5 refs.

A series of 120 cases of intracranial aneurysm is reported, in 106 of which there were signs of spontaneous haemorrhage. In the remaining 14 cases ocular signs indicated pressure on various cranial nerves. Of the 106 cases of haemorrhage, oculomotor palsies figured in 22, the third nerve being involved in 14 and the sixth in 8; in none were both affected together. Fundal haemorrhages were observed in 8 cases, papilloedema in 6, and permanent field defects in 4.

Non-bleeding aneurysms may be intracavernous, in which case oculomotor palsy, especially that due to involvement of the third nerve, may develop rapidly or, rarely, insidiously. Erosion of the sella turcica by an aneurysm may raise a suspicion of pituitary tumour, while when an arteriovenous fistula develops, cavernous sinus thrombosis or exophthalmic ophthalmoplegia of endocrine origin may be simulated. Supraclinoid aneurysm is particularly likely to produce an isolated palsy of the third nerve, and supraorbital pain is a prominent feature in such cases. Sudden changes in the visual fields are also characteristic. Angiography is by far the most valuable investigation in suspected cases.
J. E. M. Ayoub

1346. **Spontaneous Cerebellar Haemorrhage**
H. H. Hyland and D. Levy. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **71**, 315–323, Oct., 1954. 8 figs., 4 refs.

Some authors have stated that cerebellar haemorrhage occurs in circumstances similar to those causing haemorrhage elsewhere in the brain, and that the incidence of cerebral and the incidence of cerebellar haemorrhage are in the same ratio as the weights of the two structures. Over a 20-year period at the Toronto General Hospital 32 cases of cerebellar haemorrhage were seen, including 16 due to hypertensive vascular disease, 8 to angiomata, 5 to blood dyscrasias, and 3 to miscellaneous causes. During the same period and at the same hospital there were 543 cases of haemorrhage into the cerebral hemispheres and 61 of haemorrhage into the brain stem. These figures, which show that there were almost twice as many cases of haemorrhage into the brain stem as cases of cerebellar haemorrhage (the proportions being 9·6 and 5% respectively), do not support the view that the incidence of haemorrhage at a particular site is related to the weight of the structure involved.

Cerebellar haemorrhage was usually into one or other of the hemispheres, though in a few cases it involved the vermis. In 15 cases there was rupture into the fourth ventricle. Internal hydrocephalus of varying degree was common. Of the 32 patients, 31 died, the survivor being a man of 26 in whom a tentative diagnosis of "a small angioma" was made and evacuation of the clot appeared to be life-saving. Of the 5 patients with blood dyscrasias, 3 had myeloid leukaemia, one lymphatic leukaemia, and one thrombocytopenic purpura. Of the remaining 3 patients in the series, one had staphylococcal meningitis, one was suffering from methyl salicylate poisoning, and one was operated on for extruded intervertebral lumbar disk and died on the day after operation, the cerebellar haemorrhage being found at necropsy.

The symptoms in order of frequency were severe suboccipital pain (17 cases), vomiting (11), mental confusion (7), dizziness (6), ataxia, dysarthria, and incoordination (5), collapse (2), hemiplegia (1), hiccup (1), and pulmonary oedema (1). Loss of consciousness and variable neurological disturbances, especially pupillary abnormalities, were the most common findings on admission to hospital [It is interesting to note that tonic spasms usually attributed to "cerebellar fits" were not observed.] In most cases death was from respiratory failure.

The authors state that since death occurs very rapidly, and in many cases the neurological manifestations do not clearly indicate cerebellar involvement, it is difficult correctly to diagnose the condition in time for the appropriate surgical treatment to be given.
Fergus R. Ferguson

CEREBRAL TUMOURS

1347. **Visual Disturbances Associated with Gliomas of the Temporal and Occipital Lobe.** [In English]
J. Edmund. *Acta psychiatrica et neurologica Scandinavica* [*Acta psychiat. neurol. scand.*] **29**, 291–310, 1954. 36 refs.

The ocular disturbances, particularly changes in the visual fields, associated with temporal- and occipital-lobe gliomata are discussed with reference to 208 verified cases seen at Rigshospitalet, Copenhagen, between 1934 and 1952. The tumour was located in the temporal lobe in 196 cases (116 males and 80 females) and in the occipital lobe in 12. The author confirms Meyer's finding that a dissociation of the optic radiation takes place in the temporal lobe. It was noted that field defects were far more frequently found when the tumour involved the wall of the temporal horn than when it had no such relation, and that the incidence of changes in the visual field increased as the site of the tumour passed backwards with the optic radiation, so that almost all patients with an occipital-lobe tumour had a visual-field defect, usually complete hemianopia. Such a defect was also seen in almost all cases in which the tumour completely filled the temporal lobe. With smaller tumours

a quadrantic defect was frequently observed, particularly affecting the upper quadrants. The author does not agree with other workers that incongruity of the field defects is of value in determining the side of the tumour. The incidence of papilloedema increased in direct proportion to the degree of malignancy of the tumour.

[Although a list of 36 references is appended, it unfortunately omits the names of many authors referred to in the text.] *Hugh Garland*

1348. **Some Clinical Features of the Symptomatology of Gliomas of the Temporal Lobe.** [In English]
J. EDMUND. *Acta psychiatrica et neurologica Scandinavica* [*Acta psychiat. neurol. scand.*] **29**, 311–317, 1954. 4 figs.

Certain clinical features of the series of 196 verified cases of glioma of the temporal lobe discussed in the previous paper [Abstract 1347] are presented. Most of the tumours were astrocytomata (43%) or glioblastomata (39%). About 75% of the cases of glioblastoma were of less than 6 months' duration, whereas a similar proportion of the cases of astrocytoma were of longer standing. There was no notable difference between the two groups in regard to eye signs except that papilloedema was commoner with glioblastoma, but convulsions and all other epileptic phenomena were very much more commonly associated with astrocytoma. Another striking difference was the notable excess of males (70%) over females (30%) in the group with glioblastoma, compared with the approximately equal sex distribution of astrocytomata. For both sexes the incidence of glioblastoma reached a peak between the ages of 50 and 60, whereas the highest incidence of astrocytoma was at about age 30. *Hugh Garland*

1349. **Brain Tumor and Lumbar Puncture**
L. G. LUBIC and J. T. MAROTTA. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat. (Chicago)*] **72**, 568–572, Nov., 1954. 9 refs.

The authors review the results of 447 lumbar punctures carried out at the Presbyterian Hospital, New York, in 401 cases of histologically verified cerebral tumour. They note that only one untoward reaction occurred—a death probably due to uncal herniation, whereas "lumbar puncture was of aid in establishing the diagnosis of neoplasm in a large percentage of the cases". They state that "it is realised that these patients represent a selective group in that lumbar puncture is not routinely performed in patients with brain tumor, and many cases with a high degree of papilledema were not subjected to this test". However, papilloedema was present in 32% of the 401 cases, and in 25% "the diagnosis of neoplasm was substantiated by an elevated cerebrospinal fluid pressure, even though the optic discs showed no obvious papilledema".

[The only details given of the findings in these cases are the pressure readings, and it is not specifically stated by the authors what other useful diagnostic information can be obtained by lumbar puncture in cases of cerebral tumour. It is certain that in cases with frank papilloedema the dangers of this procedure outweigh its usefulness and as the authors themselves emphasize, it should never be carried out as a routine, but "only when the findings will be of aid in establishing the correct diagnosis".] *J. MacD. Holmes*

EPILEPSY

1350. **Disappearance and Migration of Epileptic Foci in Childhood**
E. L. GIBBS, H. W. GILLEN, and F. A. GIBBS. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **88**, 596–603, Nov., 1954. 6 figs., 2 refs.

The authors describe the results of follow-up studies of 143 children in whom the electroencephalogram (EEG) had shown an epileptic focus to be present in either the occipital or mid-temporal region. Records were always taken both in the waking state and during sleep. There were 45 children in whom an occipital-lobe focus had been demonstrated before the age of 9 years; re-examination after this age showed that in 18 (40%) the EEG had become normal, while in others the focus had moved to the parieto-temporal or mid-temporal region. The remaining 98 children, in whom the focus had been mid-temporal, were restudied after the age of 15 years, and in 52 cases the record had become normal. Only in 9 cases was there still a mid-temporal focus, in 15 it had moved to the anterior temporal area, while in 22 it had been replaced by 14- and 6-per-second positive spikes, which are stated to constitute "presumptive evidence of epileptic disorder in the thalamus or hypothalamus". In both groups all those patients whose EEG had become normal were also free from seizures, while in many other cases the seizures had disappeared or become significantly less frequent. [The number of patients who suffered from clinical seizures originally is not specified.]

The authors conclude that with increasing age an epileptic focus tends to "heal" before adolescence or migrate into the region in which such activity is characteristically found at the age attained, the symptomatology of the seizure changing to the type usually associated with a focus at the new site. They consider that anticonvulsant medication may usually be discontinued safely one year after the EEG has become normal; they also suggest that unless an organic lesion is demonstrated, a neurosurgical attack on occipital and mid-temporal foci is contraindicated in childhood.

[This paper is unsatisfactory for many reasons. The technique of recording is not described; presumably the authors used their routine monopolar method, but since the position of the reference electrode is not described it is impossible to be certain of the exact location of the foci which they describe. The use of the term "occipital-lobe epilepsy" to describe cases with occipital-lobe spikes is clearly unsatisfactory in the absence of clinical evidence to suggest that seizures began in the occipital lobe. Moreover, these discharges, which the authors describe as a common finding, are unfamiliar to many other workers in the field, as are the 14- and 6-per-second positive spikes of so-called thalamic or hypothalamic epilepsy. Surely, too, the use of the word

"healing" to describe the disappearance of electroencephalographic foci is to be deplored. Undoubtedly in childhood spikes which are apparently focal in origin do migrate, but the migration observed in the authors' cases might well have been demonstrable in records taken after an interval of a few days instead of several years.]

J. N. Walton

1351. **Psychological Studies of Seven Epileptic Hemiparetics before and after Hemispherectomy**

A. E. Uecker, L. A. French, and D. R. Johnson. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] **72**, 555–564, Nov., 1954. 1 fig., 30 refs.

The effect of hemispherectomy upon the convulsions and sensory and motor systems of 7 patients who had had hemiparesis from infancy, accompanied by epilepsy which did not respond to anticonvulsant therapy, has already been reported. In this paper from the University of Minnesota Hospital, Minneapolis, the authors report a study of the I.Q. and social behaviour of these patients (3 males and 4 females) before and after the operation. The patients' ages ranged from 13 to 35 years and at the time of operation their intelligence varied from idiocy to low normal. In addition to the clinical picture of hemiparesis and convulsions, there were gross abnormalities in the electroencephalogram, the pneumoencephalogram, and the carotid angiogram. The operation consisted in removal of one cerebral cortex, along with the insula, hippocampal gyrus, and the inferior medial orbital gyri. The greater part of the basal nuclei and, later, the caudate nucleus were also removed.

Although several patients seemed rather more alert after the operation, the results of intelligence tests were not markedly different from those obtained before operation. Other tests indicated slight improvement in the intellectual functioning of 2 patients who were "near normal" before operation. There was no improvement in adjustment as the result of hemispherectomy, although 2 patients were no longer subject to "temper tantrums". The authors conclude that improvement in intelligence and adjustment probably depends upon the integrity of the remaining hemisphere, and that further research is necessary before hemispherectomy can be recommended as a method of improving the mental function of epileptic hemiplegics.

E. H. Johnson

1352. **Localization of Discharge in Temporal Lobe Automatism**

W. Feindel and W. Penfield. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] **72**, 605–630, Nov., 1954. 14 figs., 21 refs.

The authors analyse the clinical features of spontaneous temporal-lobe seizures and report the results of electrical stimulation in 155 patients who were operated upon under local analgesia at the Montreal Neurological Institute. Of these patients, 121 (78%) showed some evidence of behavioural automatism, either at the outset of the attack or after preliminary psychical, sensory, or brief motor phenomena. The automatism included unresponsiveness, confusion, masticatory movements, and inappropriate but often elaborate behaviour for which the patient was later amnesic. It was clear that the automatism was sometimes ictal, but more often it was postictal. In a more detailed analysis of 50 of the cases it was found that in a few cases there seemed to be no preliminary warning sensations, but in others the phenomena which most often preceded automatism were abdominal sensations, "conscious confusion", tonic or adversive motor features, somatic sensation, cephalic sensation, or feelings of unreality—a common sequence was conscious confusion, followed by tonic or adversive motor movements, and then automatism.

Electrical stimulation of the brain at various points in and around the temporal lobe was successful in reproducing automatism and amnesia, sometimes with widespread suppression of the electrical activity of the cortex. Some of this evidence indicated that the deep mesial structures of the temporal lobe are concerned in motor responses which may be additional to those derived from the Rolandic, supplementary motor, and second sensorimotor areas. It was shown that the area responsible for the initiation of behaviour automatism is the periamygdaloid region, including the uncus, the amygdala, the ventral claustrum, and the temporoinsular cortex deep in the anterior part of the Sylvian fissure. The authors point out that this area is particularly susceptible to damage during tentorial herniation, either by direct pressure or by ischaemia due to compression of the anterior choroidal artery. This fact is consistent with their view that temporal-lobe seizures may result from incisural sclerosis due to herniation of the temporal lobe at birth.

The authors suggest that their observations support the view that the claustro-amygdaloid grey matter can be considered along with the diffuse projection systems of the thalamus and brain stem as a region capable of exerting diffuse regulatory effects on other parts of the brain. It appears that the periamygdaloid region is also concerned in the processes of memory recording and in the maintenance of the normal conscious state, both of which are clearly essential factors in the mechanism of behaviour.

J. N. Walton

1353. **Classification of the Epilepsies with Particular Reference to Psychomotor Seizures**

C. Symonds. *Archives of Neurology and Psychiatry* [*Arch. Neurol Psychiat.* (*Chicago*)] **72**, 631–637, Nov., 1954. 9 refs.

The author discusses the classification of the epilepsies in the light of recent rapid advances in our knowledge concerning the anatomical and electrophysiological background of various seizure patterns. He points out that in order to understand fully the aetiology and mechanism of any seizure it is necessary to have a clinical description of its pattern, a knowledge of the anatomical location of its site of origin, physiological data explaining its mode of spread and the activation of various parts of the brain, pathological evidence as to the nature of the underlying lesion (if any), and information concerning the ability of various drugs to control it.

The physiological data may further be divided into electrical and biochemical findings. He believes that seizures with total loss of consciousness and with generalized convulsive movements may best be referred to as major seizures, but does not feel that the term " petit mal " is now satisfactory to describe momentary seizures, in view of its use by electrophysiologists to identify those seizures which are accompanied by a 3-per-second spike-and-wave discharge in the electroencephalogram (EEG). Not all clinical seizures which are momentary are accompanied by such activity. The author suggests that such attacks are best referred to as " minimal seizures ", and that the term " minor seizure " could reasonably be used to include all attacks which do not fall into the major and minimal groups as already defined. Further, he points out that the terms major, minor, and minimal, though useful as general groupings, will yet allow for exact definition of individual seizures on clinical, anatomical, physiological, and pathological lines. In common with many recent authors he prefers the term temporal-lobe epilepsy to psychomotor epilepsy, and points out that seizures arising from foci in the temporal lobe may be major, minor, or minimal in degree, the clinical pattern of the seizure varying with the precise situation and direction of spread of the discharge. With better correlation of clinical, EEG, and pathological findings, more accurate location of the site of origin of the various types of seizure may be possible and a study of the seizures arising from anterior and posterior or deep and superficial foci may prove them to be distinctive. *J. N. Walton*

1354. **Masked Epilepsy**
H. R. E. WALLIS. *Lancet* [*Lancet*] **1**, 70–74, Jan. 8, 1955. 20 refs.

Cases are described in which epilepsy manifested itself as pain in the leg, so-called cyclical vomiting, headaches, pyrexia, and abdominal pain. This type of epilepsy is fairly common though often unrecognized, and many cases of cyclical vomiting and migraine may prove to be epileptic. The term " masked epilepsy " should be extended to include these phenomena. Treatment with phenobarbitone is usually successful.—[Author's summary.]

CRANIAL NERVES

1355. **Cortisone Treatment of Bell's Palsy**
D. TAVERNER. *Lancet* [*Lancet*] **2**, 1052–1054, Nov. 20, 1954. 9 refs.

Results are reported of a trial of the effect of cortisone on the incidence of denervation of the facial muscles in Bell's palsy. The criteria on which the diagnosis of Bell's palsy was based were: (1) sudden onset of paralysis of all the muscles of one half of the face; (2) absence of evidence of involvement of the central nervous system; and (3) absence of any symptom or sign of disease of the ear or posterior fossa. A series of 26 patients with Bell's palsy were examined and electromyograms recorded before treatment was begun, and none showed evidence of denervation. Of the 26 patients, 14 received by mouth 200 mg. of cortisone acetate daily for 3 days, 100 mg. daily for 3 days, and 50 mg. daily for 2 days; the remaining 12 patients, who served as controls, received lactose. In 4 of the treated group and in 4 of the controls denervation developed; the remaining patients in both groups recovered. The mean duration of the palsy in the treated patients who recovered was 63 days and in the control patients it was 69 days.

The author concludes that cortisone in the dosage employed in this investigation has no effect on the course of Bell's palsy. *L. G. Kiloh*

1356. **Trigeminal Neuralgia: Comparison of the Various Surgical Methods to Combat Trigeminal Neuralgia, Especially the Spiller Frazier and the Dandy Method.** [In English]
P. R. M. J. HANRAETS. *Folia psychiatrica, neurologica et neurochirurgica Neerlandica* [*Folia psychiat. (Amst.)*] **57**, 382–404, Oct., 1954. 2 figs., 35 refs.

The results of various surgical procedures in the treatment of trigeminal neuralgia are reviewed in this paper from the St. Ursula Clinic, Wassenaar, Holland. The author holds that injection of the ganglion with alcohol is indicated only in patients in poor physical condition or young patients experiencing a first attack, and Sjöqvist's operations of tractotomy and mesencephalotomy only in young, fit patients with pain in the first or second division of the trigeminal nerve. In 1952 Taarnhøj described an operation to decompress the Gasserian ganglion without interfering with its fibres, the operation being performed both intradurally and extradurally. This is stated to give immediate relief of pain in 90% of cases, but the author notes that Taarnhøj himself reported late recurrence of pain in several cases.

The author then discusses the two most commonly used techniques: (1) postganglionic root section, as described by Spiller Frazier, in which the ganglion is approached by the temporal route either intradurally or extradurally; and (2) section of the trigeminal trunk at the pons, as described by Dandy, in which a unilateral cerebellar approach is used. He states that not only was the operation of Spiller Frazier the first to be effective in the relief of trigeminal neuralgia, but it also carries a very low mortality rate and the recurrence rate is low. It has, however, two disadvantages—namely, the high incidence of paraesthesiae after operation (20 to 50%), and the tendency for corneal complications to develop (in 7 to 15% of cases). The operative mortality with Dandy's technique apparently varies considerably in different clinics (0·5% in Dandy's series, 12% in the author's clinic). However, the recurrence rate is lower than it is with the Spiller Frazier operation and there is little or no anaesthesia dolorosa. Paraesthesiae and corneal complications occur in a very few patients only.

The author sums up by stating that Sjöqvist's operation is less frequently performed than it used to be, and that while there is a marked preference for the Spiller Frazier method, this should not be regarded as the method of choice, because Dandy's operation offers many advantages. *J. V. Crawford*

Psychiatry

1357. **Clinical Significance of the Photomyoclonic Response in Psychiatric Patients**
C. SHAGASS. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **6**, 445–453, Aug., 1954. 2 figs., 12 refs.

In addition to inducing the simple occipital response in the electroencephalogram (EEG), intermittent photic stimulation with repeated flashes of light may in some individuals give rise to rhythmic muscular jerking, the photomyoclonic response, which may be limited to the palpebral region or spread generally throughout the body. Such a response was found to some degree in 83 (20·2%) of 411 psychiatric patients admitted to the Allen Memorial Institute (McGill University), Montreal, and in 3 (10%) of 30 normal control subjects; this is not a significant difference.

In the psychiatric patients no correlation was found between the occurrence of this response and any particular psychiatric disorder, nor was it related to age. There was, however, some degree of correlation with a history of " deviant cerebral excitability "—namely, a personal and family history of spontaneous fits or of recent electric convulsion or insulin therapy, or a history of barbiturate addiction, intoxication, or coma. The stronger such a history, the more likely was it that the photomyoclonic response would spread widely. The response was more commonly observed in females than in males, and an abnormal resting EEG was more frequently present in those giving the photomyoclonic response.

W. A. Cobb

1358. **The Prognostic Significance of Conditioned Reflex Hypoglycaemia in Mental Disorders.** (О прогностическом значении условной гипогликемии при психических заболеваниях)
N. P. STATSENKO. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **54**, 767–768, Sept., 1954. 3 refs.

Working at the Omsk Psychoneurological Hospital and Medical School, the author studied the prognostic significance of conditioned reflex hypoglycaemia in 50 psychiatric patients, 38 of whom were schizophrenic. Daily injections of insulin were given for 20 to 25 days and were then replaced by similar injections of saline. The blood sugar level was estimated at intervals during the 2½ hours after the injection of insulin or saline, and conditioned reflex hypoglycaemia was considered to be present if the injection of saline caused the level to fall by more than 10 mg. per 100 ml.

Reflex hypoglycaemia occurred in all cases in which a satisfactory clinical remission of the psychiatric condition subsequently occurred, and in some others. Patients with schizophrenia of several years' standing showed the least response. The test is therefore considered to be of some prognostic value, a positive result suggesting a greater probability of remission. It was observed that the symptomatology of conditioned reflex hypoglycaemia, even when marked, differed from that of hypoglycaemia induced with insulin in that there was less sweating and less change in the pulse and respiration rates, and in that coma never occurred. *L. Crome*

1359. **Psychiatric Illness in the Elderly. A Follow-up Study**
B. A. O'CONNELL. *British Medical Journal* [*Brit. med. J.*] 2, 1206–1208, Nov. 20, 1954. 16 refs.

During 1951 a total of 119 patients aged 65 years or more were admitted to the Crichton Royal Infirmary, Dumfries, suffering from mental disorder, and in this paper the author discusses the treatment and subsequent history of these cases. The patients were grouped as follows: affective disorder, 33; senile dementia, 51; cerebral arteriosclerosis, 13; and various disorders including schizophrenia, essential delirium, alcoholism, and dementia paralytica. All were followed up at intervals of 6 months, one year, and 2 years.

It was found that in cases of senile dementia and cerebral arteriosclerosis, which together accounted for about one-half of the total, the prognosis was relatively poor. By contrast, affective disorder was a benign condition which often responded satisfactorily to electric convulsion therapy (E.C.T.). It is emphasized that affective disorder in the elderly must be differentiated from the organic psychoses so that the appropriate treatment may be given. Age alone is no bar to E.C.T., especially when relaxants are given; moreover, with such treatment the stay in hospital is reduced and the recovery rate is high. *J. B. Stanton*

1360. **Experience in the Management of Patients Medically Addicted to Narcotics**
M. RAYPORT. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **156**, 684–691, Oct. 16, 1954. 10 refs.

Of 1,020 male patients admitted consecutively to the U.S. Public Health Service Hospital, Lexington, Kentucky, an institution for the treatment of narcotic addiction, 141 were regarded as medical addicts—that is, " persons of normal nervous constitution to whom an opiate has been prescribed . . . to relieve the suffering of some prolonged physical condition ". The author discusses the management of these cases, which, according to the underlying illness for which the narcotic was originally prescribed, fell into three groups. The first group of 89 patients received opiates for an illness from which they later recovered. Nearly one-third of these were chronic alcoholics, and all had given up alcohol almost immediately after the narcotic was prescribed. The treatment of this group was similar to that given to " non-medical " addicts. The second group of 2

patients received a narcotic for a curable condition (renal calculi in one and recurrent migraine in one). Surgical treatment was successful in both cases. The third group of 50 addicts were suffering from incurable disease, including cardiovascular, respiratory, and neurological disorders and bone and joint diseases. In these cases "methadone" (amidone) was gradually substituted for the narcotic, the period of substitution ranging from one to 15 days. Over 40 of these patients claimed to feel well after they had abstained from taking a narcotic for 100 days.

The author believes that many medical addicts would be willing to undergo this withdrawal treatment and that the attending physician could carry it out quite safely, advising admission to an institution only if such treatment failed. *L. G. Kiloh*

1361. **The Virus Factor in the Pathogenesis of Schizophrenia.** (Вирусный фактор в патогенезе шизофрении)
G. Y. Malis and S. I. Dolgikh. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **54**, 728–731, Sept., 1954.

The authors, working at the Sukhumi Medico-biological Station in the Georgian S.S.R., applied the so-called "AVB" reaction to the blood of schizophrenic patients. This reaction is based on the observation that the adsorption of a virus on to certain bacteria renders the latter agglutinable by serum containing antibodies against the virus concerned. The results indicated the periodic appearance in the blood in these cases of a specific virus antigen of unknown origin and of antibodies to this antigen. *L. Crome*

1362. **Virus-like Bodies in Schizophrenia.** (О вирусоподобных тельцах при шизофрении)
M. A. Morozov. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **54**, 735–740, Sept., 1954. 8 figs.

The author has examined nasopharyngeal swabs and samples of cerebrospinal fluid from 29 schizophrenic patients by ordinary and dark-field microscopy at the Institute of Virology, Moscow. He found elementary bodies in 19 of the cases. These bodies were not present in specimens from a control group of 19 patients suffering from other conditions. He concludes that this finding suggests a probable virus aetiology of schizophrenia, further proof of which should now be sought by the usual virological methods. *L. Crome*

1363. **Clinical Observations on the Treatment of Schizophrenia with Dimedrol. Preliminary Communication.** (Клинические наблюдения над лечением шизофрении димедролом (Предварительное сообщение))
V. M. Shpak. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **54**, 769–772, Sept., 1954. 11 refs.

The antihistamine preparation "dimedrol" (the chemical constitution of which is given as dimethylaminoethylbenzhydrol hydrochloride) was tried in the treatment of 30 schizophrenic patients. It was usually given by mouth or subcutaneously in doses of 0·05 to 0·5 g. 2 to 4 times a day (sometimes being combined with bromides and hypnotic drugs (bromvaletone, carbromal, or urethane) at night) as part of a scheme of treatment which often included sleep therapy and insulin shock. A number of patients underwent a temporary remission and in 4 cases a more lasting remission was obtained—up to 6 months at the time of the report. *L. Crome*

1364. **A Comparative Study of the Effect of Mephenesin and Placebo on the Symptomatology of a Mixed Group of Psychiatric Outpatients**
J. L. Hampson, D. Rosenthal, and J. D. Frank. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **95**, 170–177, Oct., 1954. 9 refs.

The comparative efficacy of mephenesin and of a placebo in the treatment of 35 patients whose psychiatric disorder ranged from "psychoneurotic reactions to a schizophrenic type of illness" was investigated at the Johns Hopkins University School of Medicine. Mephenesin was given in a dosage of 3 g. daily for a fortnight and 9 g. daily for a similar period, alternating with a placebo which was given under similar conditions and for a similar period. Patients were seen every fortnight by the same doctor, who assessed the response to treatment on a simple 4-point scale, making use of a questionary which elicited information about 34 symptoms. By means of subscales of the 4-point scale, symptoms were grouped into those which were somatic and those which were psychic in origin. The Bender Gestalt Test was used to determine whether mephenesin had any effect on tremor. Only 17 patients completed the 8-week course of treatment.

During the first part of the trial 15 patients received a placebo and 9 received 3 g. of mephenesin daily. In patients receiving the placebo there was a statistically significant reduction in symptoms, but in those receiving mephenesin there was only slight alleviation. Muscular symptoms responded better than did cardiovascular or gastrointestinal symptoms, and depressed patients benefited more than those with anxiety symptoms. This initial response confirmed Wolf's observation (*J. clin. Invest.*, 1950, **29**, 100; *Abstracts of World Medicine*, 1950, **8**, 346) that the mere giving of drugs often has an alleviating effect, regardless of their pharmacological properties. A dosage of 9 g. daily of mephenesin appeared to have more effect than one of 3 g., but the difference was too small to be significant. The larger dosage was not, however, any more effective than the placebo, and in 13 out of 17 cases it caused unpleasant side-effects. No improvement in tremor as measured by the Bender Gestalt Test was noted. *Richard de Alarcón*

1365. **Succinylcholine Chloride in Electroshock Therapy. III. Oxygen Consumption and Arterial Oxygen Saturation**
W. P. Wilson, J. B. Hickam, W. K. Nowill, and R. Frayser. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] **72**, 550–554, Nov., 1954. 1 fig., 8 refs.

Dermatology

1366. **On the Aetiology of Chronic Pemphigus and Dermatitis Herpetiformis.** (Sulla etiologia del pemfigo cronico e della dermatite erpetiforme)
N. MELCZER. *Archivio italiano di dermatologia, sifilografia e venereologia* [*Arch. ital. Derm.*] **26**, 321–332, 1954. 9 figs., 42 refs.

The author, who writes from the University Dermatological Clinic, Pécs, Hungary, believes that pemphigus vulgaris and dermatitis herpetiformis are diseases caused by identical viruses. After briefly reviewing the literature on the subject he describes the results of the experimental inoculation of chick embryos with fluid from the bullae of affected individuals. He claims that the lesions produced in the skin as bullae and in the central nervous system resembled those of the disease in human beings. He comes to the conclusion that pemphigus vulgaris and dermatitis herpetiformis are one and the same viral disease of the central nervous system, although the manifestations of the latter are less serious than those of the former.

[If the results of this investigation can be confirmed by other workers they may be of great importance.]

S. T. Anning

1367. **Dermatological Aspects of Cretinism**
T. BUTTERWORTH. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph. (Chicago)*] **70**, 565–575, Nov., 1954. 2 figs., 2 refs.

The characteristics of the skin of the cretin are described in this paper from the University of Pennsylvania. Usually the skin of the cretin is cool, coarse, and dry, and either bronzed or pasty-white in colour. The hair of the head is coarse, and body hair is sometimes scanty. The nails are normal except for the absence of the lunula. In most cases there is an excess of fat about the face, nape of the neck, supraclavicular region, hips, and mons veneris. The cretin tolerates cold poorly, and frequently wears wool in warm weather. When the hand of a normal individual is placed in very cold water there is generally a rise in blood pressure; in the cretin either the rise is slight or no rise is recorded, and even after administration of thyroid extract the normal reaction to cold is not observed. An abnormally long exposure to ultraviolet rays is necessary to produce erythema and pigmentation in cretins; this exposure time is reduced when thyroid extract is given. The triple response to firm stroking of the skin with a blunt instrument is not obtained in many cretins, even after treatment; on the other hand, intracutaneous injection of histamine phosphate produces a normal weal. The cretin perspires much less than the normal subject. Histological examination shows that the epidermis and corium are abnormally thin and that cutaneous appendages are scanty; other features are hyperkeratosis, thickness of the granular layer, fragmentation of collagen bundles, and marked degeneration of the elastic tissue. Generally there is slight oedema. After treatment the histological appearances more nearly resemble those of normal skin.

E. Lipman Cohen

1368. **Investigations into the Action of Nicotinic Acid Ester on Blood Vessels and Its Application in Testing the Function of the Vessels of the Skin.** (Untersuchungen über die Gefässwirkung der Nikotinsäureester und ihre Anwendung zur Funktionsprüfung der Hautgefässe)
W. SCHULZE. *Dermatologische Wochenschrift* [*Derm. Wschr.*] **130**, 1238–1244, 1954. 1 fig., 12 refs.

It is known that the local application of nicotinic acid ester to the skin is followed after about 10 minutes by powerful vasodilatation of the cutaneous vessels which lasts some 20 to 30 minutes and is unaccompanied by any general side-effects. The reaction varies in degree from follicular erythema to the full triple response of Lewis, depending on the concentration of the drug. It is possible to depress the reaction by administering antihistamine drugs.

In this paper from the University Skin Clinic, Freiburg im Breisgau, a method is described for testing the function of the cutaneous vessels by gently applying the lowest active concentration of a solution of nicotinic acid ester to a standardized area of the skin. The average lowest useful concentrations were found to lie between 0·003 and 0·03%. It was shown to be of the greatest importance to standardize the skin temperature before carrying out the test, as even a difference of 2° or 3° C. alters the threshold by 3 to 5 times. It was noted during these experiments that the skin response was occasionally reversed, presenting a picture of local pallor; but even in these cases the skin temperature was shown to be higher than before the reaction started.

G. W. Csonka

1369. **Differentiation and Treatment of Eczemas of the Eyelids**
F. H. THEODORE. *Transactions of the American Academy of Ophthalmology and Otolaryngology* [*Trans. Amer. Acad. Ophthal. Otolaryng.*] **58**, 708–723 Sept.–Oct., 1954. 6 figs. 40 refs.

The two main types of eczema of the eyelids are allergic eczematous dermatitis and infectious eczematoid staphylococcal dermatitis. The former is a contact allergy produced by locally applied drugs, cosmetics, or other irritants. Non-protein substances may combine with the body tissues to form conjugates which act as antigens. The allergic response results in itching, papillary conjunctivitis, eosinophilia of the conjunctival sac, and eczema of the skin of the lids. The patch test is a more useful diagnostic aid than the intracutaneous test, as in these cases the allergic process is situated in the epidermis. The only method of treatment is to eliminate

the cause: antihistaminics are useless. The local application of cortisone may allow the administration of an allergenic drug to be continued when necessary.

In infectious eczematoid staphylococcal dermatitis the eczema results from chronic staphylococcal infection around the eyes or on the hands. Superficial epithelial erosions of the lower half of the cornea are pathognomonic, and other characteristic features are the presence of blepharitis or meibomitis, the presence of staphylococci in cultures from the lid margins or conjunctiva, and the absence of conjunctival eosinophilia. The eczema appears to result from the dermonecrotizing factor of the staphylococcal toxin combined with an allergy to other staphylococcal products. The aim of treatment is to eliminate the infection and to desensitize the patient, when indicated, by the injection of staphylococcal toxoid or vaccine. Sodium propionate (10%) applied locally is recommended in the early treatment, and the skin and any fissures should be painted with 2% silver nitrate at infrequent intervals. Toxoid and vaccine treatment is reserved for those cases wherein excessive allergy is present, as revealed by a severe reaction to the intradermal injection of dilute toxoid.

In addition, a non-specific eczema of the lids may occur in atopic dermatitis, neuro-dermatitis, psoriasis, and seborrhoeic dermatitis. The treatment, which must be carried out in several stages, is discussed.

Douglas Langley

1370. **A Case of Bromoderma Vegetans.** (Un caso de brómides vegetantes)
J. BIGNÉ and J. GUILLÉN. *Actas dermosifiliográficas* [*Act. dermo-sifiliogr.* (*Madr.*)] **46**, 44–48, Oct., 1954.

The case is described of a 6-month-old, breast-fed child who, after a total dose of 3·15 g. of bromide had been administered in a cough mixture over the period of 5 days, developed a bromide rash of typically exuberant character. The presence of bromine in the urine was demonstrated by Belote's reaction (in which blotting paper coloured yellow with fluorescein solution and then dried is moistened with acetic acid and placed in the urine, a change of colour from yellow to rose denoting the presence of bromine). The condition is discussed, and the suggestion is made that the sensitivity of breast-fed infants to bromides is attributable to the low salt content of human milk.

[No references are given to the authorities cited in the text.] *Eric Dunlop*

1371. **Histopathologic Correlation of Lesions of Papular Urticaria and Positive Skin Test Reactions to Insect Antigens**
B. SHAFFER, C. JACOBSON, and H. BEERMAN. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph.* (*Chicago*)] **70**, 437–442, Oct., 1954. 3 figs., 20 refs.

Specimens from skin lesions and from the site of injection of insect antigens in patients with papular urticaria, and also specimens from insect bites in healthy subjects, were examined histologically at the University of Pennsylvania. It was found that the early or urticarial type of lesion in papular urticaria and the skin immediately after injection of insect antigen or an insect bite had many features in common—for example, the presence of oedema and of an infiltrate consisting mainly of lymphocytes and eosinophils. The late or papular lesions of papular urticaria were of two types—the inflammatory, in which the reaction to insect antigen resembled the tuberculin type of reaction, with a dense infiltration of lymphocytes and eosinophils; and the non-inflammatory, in which the infiltrate consisted almost entirely of lymphocytes.

The authors consider that their findings add support to the view that papular urticaria is often an allergic reaction to the bites of insects. *Kate Maunsell*

1372. **Topical Use of Hydrocortisone and Hydrocortisone–Neomycin Ointments in Allergic Dermatoses**
S. FRIEDLAENDER and A. S. FRIEDLAENDER. *Journal of Allergy* [*J. Allergy*] **25**, 417–428, Sept., 1954. 20 refs.

Local application of hydrocortisone ointment was tried at the Wayne University College of Medicine, Detroit, in the treatment of 159 patients suffering from atopic dermatitis, contact dermatitis, and various dermatoses. The free alcohol or the acetate of hydrocortisone was used in concentrations of 2·5 and 1%. Striking or moderate improvement was observed in more than 80% of the patients within 24 to 48 hours, the improvement being more pronounced in excoriated, papulovesicular, scaling, and lichenified lesions than in urticarial or deep vesicular eruptions. In chronic disorders, however, the improvement lasted only so long as the ointment was applied, relapse occurring usually within 2 or 3 days. The ointment containing the free alcohol was as effective as that containing the acetate, and in many cases the 1% concentration was sufficient. In some cases maintenance therapy was possible with the 1% ointment, while in others tolerance developed. Systemic treatment was necessary in patients with generalized eruptions. The authors found that the addition of 0·5% neomycin to the ointment improved the results in those cases in which there was an infectious element [but the evidence presented for this conclusion is not convincing]. *H. Herxheimer*

1373. **Cattle Ringworm**
A. J. ROOK and W. FRAIN-BELL. *British Medical Journal* [*Brit. med. J.*] **2**, 1198–1200, Nov. 20, 1954. 13 refs.

Cattle ringworm is caused predominantly by *Trichophyton mentagrophytes* and *Tr. discoides*, the latter being the commonest cause in Britain, and stall-fed cattle are more often affected than animals out at grass. The fungus survives for long periods in the debris around stables and for still longer periods on the woodwork, especially of damp, dark cowsheds. No reliable figures are available of the incidence of cattle ringworm in human beings, but the authors describe 39 cases which were referred to various dermatological clinics in South Wales over a 3-year period, during which time some 12,000 new patients were examined. The majority of the authors' patients gave a history of a direct contact with infected cattle. In traumatized human skin the lesions may appear a few days after infection; in the

absence of trauma the incubation period is longer. The peak incidence occurs during the winter months, coinciding with the period of maximum incidence among cattle. When the inflammatory reaction is very severe sulphonamides should be given instead of penicillin because, theoretically, the patient who is sensitive to trichophytin may also be sensitive to penicillin.

Kate Maunsell

1374. **Relationship between Ritter's and Leiner's Diseases**

H. N. COLE, R. G. HODGES, and F. F. SILVER. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph. (Chicago)*] **70**, 443–451, Oct., 1954. 3 figs., 16 refs.

After reviewing the clinical and pathological features of Ritter's disease and of Leiner's disease, the authors discuss the histological appearances of the skin in 2 cases of Ritter's disease and one of Leiner's disease, and the necropsy findings in one of the former, the cases being seen at three hospitals in Cleveland, Ohio. Their observations lead them to conclude that Leiner's disease is a modified subacute form of Ritter's disease, this view being based on the close similarity of the clinical features and the lack of distinguishing histological characteristics. They suggest that staphylococcal infection, with concomitant vitamin-B deficiency, is concerned in the aetiology.

Kate Maunsell

1375. **Parapemphigus (" Pemphigoid ") and Pemphigus Vulgaris.** (Parapemphigus (" pemphigoid ") en pemphigus vulgaris)

J. R. PRAKKEN and M. J. WOERDEMAN. *Nederlandsch tijdschrift voor geneeskunde* [*Ned. T. Geneesk.*] **98**, 3127–3135, Oct. 30, 1954. 11 figs., 20 refs.

While the separation of the condition described as " bullous pemphigoid " by Lever (*Medicine*, 1953, **32**, 1), and as " pemphigoid " by Rook and Waddington (*Brit. J. Derm.*, 1953, **65**, 425; *Abstracts of World Medicine*, 1954, **15**, 428) from pemphigus vulgaris is confirmed by the present authors on the basis of observations made at the University Skin Clinic, Amsterdam, since 1947, they have found that the two conditions cannot always be differentiated and therefore suggest the alternative name of " parapemphigus ". The essential histological differences distinguishing pemphigoid are the absence of acantholysis and the subepidermal position of the bullae. The fact that in pemphigus vulgaris the bullae are intraepidermal and generally suprabasal explains the greater tendency to spread and break down which is seen in this condition.

R. Crawford

1376. **Histology of Lupus Erythematosus**

F. A. ELLIS and W. R. BUNDICK. *Archives of Dermatology* [*Arch. Derm. Syph. (Chicago)*] **70**, 311–324, Sept., 1954. 3 figs., 7 refs.

From a review of the literature it does not appear to be agreed that chronic discoid lupus erythematosus can be differentiated from disseminated acute or subacute lupus erythematosus on histological examination of biopsy material from a skin lesion. In a series of 213 cases of lupus erythematosus (acute in 25, subacute in 25, and chronic in 163) the authors found an excellent correlation between the histological appearances and the clinical diagnosis. The histological features which were of most value in the differential diagnosis were: atrophy of the epidermis with severe oedema (seen in the acute form of the disease) and epidermal thickening, acanthosis, plugging, and infiltration (seen in the chronic form). In the subacute form the histological appearances were similar to those of the acute form except that there was less oedema. The authors were unable, however, to establish an absolute distinction between the three phases.

(One of the contributors to the discussion of this paper described a case of long-standing discoid lupus erythematosus, in which death was due to an unrelated cause and necropsy revealed lesions in the spleen which were typical of systemic lupus erythematosus. Still another contributor referred to the development in some cases of both chronic discoid and acute lupus erythematosus of a delicate line or zone of fibrinoid degeneration along the epidermal basement membrane.)

Bernard Lennox

1377. **Epithelioma Cuniculatum. A Variety of Squamous Carcinoma Peculiar to the Foot**

I. AIRD, H. DAINTREE JOHNSON, B. LENNOX, and A. G. STANSFELD. *British Journal of Surgery* [*Brit. J. Surg.*] **42**, 245–250, Nov., 1954. 16 figs., 8 refs.

Epithelioma cuniculatum is the term used for a well-defined epithelial tumour which burrows deeply into the plantar surface of the foot among the flexor tendons, producing many sinuses opening separately on the surface of the tumour. It does not destroy bone, tendon, nerve, or any important structure, but nevertheless eventually reaches the dorsum of the foot. In this paper from the Postgraduate Medical School and the Royal Free Hospital, London, the authors describe 2 cases of epithelioma cuniculatum and one pathological specimen from a case for which no clinical details were available.

The patients were men aged 64 and 71 years respectively [their occupation and social environment are not stated]. The naked-eye and microscopical features of the 3 specimens were closely similar. The tumour was situated on the anterior part of the plantar surface of the left foot in one case and the right in the other. It was squashy in consistence and on pressure a sickly-smelling, greasy sebum oozed from it. The tumours had been present for more than a year in both cases. Biopsy examination was of no help in diagnosis and a search for possible infective organisms proved negative. One tumour had recurred after local removal.

In one case mid-leg amputation was performed. This was thought to be too radical for the second case and conservative local treatment was tried for a year. When, however, the inguinal lymph nodes became enlarged a Syme's amputation was carried out. No cancer cells were found in the lymph nodes. In neither case have metastases occurred up to 3 years after amputation of the limb.

The authors consider that the tumour is a low-grade squamous carcinoma, modified by extreme keratinization and the effects of pressure.

W. Skyrme Rees

Paediatrics

1378. **Anaemia of Newborn following Anterior Placenta Praevia**

N. R. Butler and J. D. Martin. *British Medical Journal* [*Brit. med. J.*] **2**, 1455–1457, Dec. 18, 1954. 8 refs.

The authors draw attention to the risk of anaemia in the newborn as a result of incision of the placenta in performing Caesarean section. This occurred in 5 out of 19 babies delivered by lower-segment Caesarean section for anterior placenta praevia at University College Hospital, London, between 1949 and 1952. By contrast, no case of anaemia followed the performance of Caesarean section, carried out for other reasons, on 235 occasions in the same period, nor was the baby affected in 7 cases of placenta praevia delivered by the vaginal route.

The relevant obstetrical literature is reviewed. The anaemia in these cases is due to haemorrhage from the placenta before delivery and, as recommended by Macafee (*J. Obstet. Gynaec. Brit. Emp.*, 1945, **52**, 313), may be prevented by making a stab wound into the lower uterine segment followed by manual stretching of the wound, or by incising the uterus slightly higher than usual. If anaemia occurs it must be recognized early—taking into account the high haemoglobin concentration in the peripheral blood of the newborn—and treated by immediate transfusion. As haemodilution may not occur for several hours after haemorrhage the serial determination of haemoglobin levels may be necessary from birth. *A. Paton*

1379. **Leprechaunism. A Euphuism for a Rare Familial Disorder**

W. L. Donohue and I. Uchida. *Journal of Pediatrics* [*J. Pediat.*] **45**, 509–519, Nov., 1954. 16 figs., 1 ref.

The authors describe a new syndrome, genetically determined and characterized by "elfin" facies, hirsutism, and multiple endocrine abnormalities, for which they suggest the term "leprechaunism". The 2 cases described were in sisters, the first and last children in a family of 4. The other 2 children, a boy and a girl, were normal. The mother had also had 3 miscarriages. The parents were blood relations, the father being the son of a first cousin of the mother. Both children weighed less than 4 lb. (1·8 kg.) at birth, one being born at full term and the other by Caesarean section after 7½ months' gestation. Both failed to gain weight, and one died at the age of 46 days and the other at the age of 69 days.

At necropsy there was moderate facial hirsutism and excessive lanugo. The eyes were prominent and widely spaced, the ears large and low-set, the clitoris and labia enlarged, and the abdomen distended. In the liver there were sharply circumscribed patches of swollen cells with foamy vacuolization and extensive deposition of glycogen. In the pancreas the islets of Langerhans showed great hyperplasia and the insulin content was 6 times the normal value. In the pituitary gland the number of basophil cells seemed to be increased and some of the eosinophil cells showed depletion of their granules. The ovaries were large and showed marked follicular maturation and cyst formation without luteinization. The breasts showed glandular hyperplasia. The kidneys were double the normal size and showed diffuse dilatation of the tubules due to plugging of the collecting tubules with conglomerate masses of some granular, calcium-containing material.

It is presumed that a recessive gene is responsible for this condition, no other cases of which appear to have been reported. *C. O. Carter*

1380. **Complications of Myocarditis in Children**

O. Saphir and M. Field. *Journal of Pediatrics* [*J. Pediat.*] **45**, 457–463, Oct., 1954. 3 figs., 4 refs.

For a study of the complications of myocarditis in children the authors chose 15 out of a total of 45 cases which came to necropsy at Michael Reese Hospital, Chicago, between 1946 and 1952. These 15 were chosen because the myocarditis was not associated with any disease—for example, poliomyelitis—which is known to cause myocarditis. In these 15 cases of isolated (or Fiedler's) myocarditis the complications were undoubtedly due to the myocarditis itself.

The outstanding finding was the presence of minute multiple emboli in the coronary arteries and cerebral vessels, and also in other organs. The source of these emboli appeared to be small mural thrombi in the heart, although these were actually found in only 3 cases. The authors consider that more would have been found had whole hearts been available for examination. The cause of the mural thrombi was obviously the inflammatory changes close to the endocardium producing subendocardial oedema or even localized foci of mural endocarditis.

From an analysis of the relevant case histories the authors conclude that multiple emboli constituted a serious complication contributing to the death of the patient. *Marianna Clark*

1381. **Interstitial Pneumonia of Infants Caused by *Pneumocystis carinii*.** (Über die durch *Pneumocystis carinii* verursachte interstitielle Pneumonie der Säuglinge)

O. Jírovec. *Monatsschrift für Kinderheilkunde* [*Mschr. Kinderheilk.*] **102**, 476–485, Nov., 1954. 2 figs., bibliography.

The discovery of the protozoon *Pneumocystis carinii* as a constant finding in interstitial plasma-cell pneumonia was the result of the author's collaboration with Vaněk, and in the present paper he reviews very fully his own work on the subject and that reported in the literature. He describes the morphology of the organism and reports the observation of the formation within it of a highly

refractile, Gram-positive, but Feulgen-negative substance during sporogony. There is no intracellular cycle, although this may be simulated by phagocytosis. The opinion of some workers that *P. carinii* is a yeast is considered to be erroneous, and the author is convinced that it is the causative organism of interstitial plasma-cell pneumonia and not merely an incidental saprophyte. *Pneumocystis* has repeatedly been observed as a saprophyte in adults and older children, and the factors predisposing to manifest disease are discussed. The incidence of the disease has increased during the past few years and it is estimated that at least 1,000 infants died of it in the period 1952–3 in Central Europe. [So far, only one case has been reported outside the European continent—in Great Britain (Baar, *J. clin. Path.*, 1954, 7, 169).] For histological diagnosis the use of trichrome, Giemsa, and Gram–Weigert stains and the periodic-acid–Schiff reaction are recommended, Giemsa being most suitable for imprints. A complement-fixation test and a skin sensitivity test with saline extracts of infected lungs are still in the experimental stage; the latter, being non-specific, is without diagnostic value, but may be helpful in the assessment of latent infection in adults.

The symptoms and pathological findings are reviewed in detail. According to Vaněk the invasion by a few protozoa of the alveoli in susceptible infants is followed by immigration of alveolar macrophages with a few polymorphonuclear leucocytes, the occasional formation of hyaline membranes, massive interstitial cellular infiltration, plugging of the terminal air spaces by the characteristic "honey-comb" masses, and hyperplasia of the "alveolar epithelium". Recovery, if it takes place, is complete, and only exceptionally has scarring been observed. The incubation period is 2 to 10 weeks, the disease being spread mainly through infants suffering from pneumocystosis and hospital personnel with latent infection. Spread by domestic animals seems to be rare. Various types of treatment have been recommended, but the results are difficult to assess at the present time.

[This paper contains a wealth of information from an authoritative source, and an extensive bibliography is appended.] *H. S. Baar*

1382. **The Treatment of Interstitial Plasma-cell Pneumonia of Young Infants and Premature Babies.** (Zur Therapie der interstitiellen plasmacellulären Pneumonie junger Säuglinge und Frühgeborener)
M. Maneke. *Monatsschrift für Kinderheilkunde* [*Mschr. Kinderheilk.*] **102**, 485–487, Nov., 1954. 17 refs.

The aetiology of interstitial plasma-cell pneumonia and the role of *Pneumocystis carinii* are regarded by the author as still debatable. At the University Children's Clinic, Marburg, 8 infants with the disease were treated with a combination of a fungistatic and an antibiotic. The fungistatic "novex" (2 : 2-dioxy-5 : 5-dichlorodiphenylsulphide) was given as an aerosol and its acetyl ester by mouth, and either oxytetracycline or aureomycin by mouth. Of the 8 infants treated in this way, 6 recovered, one was admitted moribund, and one died of massive aspiration after having shown signs of recovery. Of 8 infants treated previously with aureomycin alone or with mepacrine and emetine, all died.
H. S. Baar

1383. **Glycogen Storage Disease of the Liver. I. Clinical Studies during the Early Neonatal Period**
J. L. Schulman and P. Saturen. *Pediatrics* [*Pediatrics*] **14**, 632–645, Dec., 1954. 10 figs., 6 refs.

Since 1948 3 newly born children, 2 of them siblings, have been seen at the Jewish Hospital, Brooklyn, suffering from extreme tachypnoea and hepatomegaly. Numerous investigations were carried out on these patients, but the only relevant findings were those of a low carbon dioxide combining power, a low serum phosphate content, and a high serum lipid level. Determination of the blood sugar concentration was not possible in the first case, the baby dying 17 hours after admission to hospital. The diagnosis was missed at the time, because the necropsy specimen of liver tissue was stained with haematoxylin and eosin only, which showed enlarged liver cells with gross vacuolization. In the light of later findings, however, it is considered most probable that this was a case of glycogen storage disease.

The 2 other children survived after treatment with large, slow, intravenous infusions of 5% dextrose with M/6 sodium lactate. Biopsy specimens of liver stained with Best's carmine revealed the presence of glycogen in the vacuoles. Glucose tolerance tests and the poor response to adrenaline confirmed that there was a grave defect of carbohydrate metabolism. Hyperlipaemia and hypoglycaemia persisted, but gave rise to no symptoms. Several months later the patients were examined electroencephalographically before and after a milk feed, during which the blood sugar level rose from 21 mg. per 100 ml. to 128 mg., but the electroencephalogram in both cases was essentially normal. The authors suggest that some unusual mechanism for the maintenance of cerebral metabolism during the periods of profound hypoglycaemia may be present in these cases.
L. H. Worth

1384. **Glycogen Storage Disease of the Liver. II. Enzymic Studies**
G. T. Cori and J. L. Schulman. *Pediatrics* [*Pediatrics*] **14**, 646–650, Dec., 1954. 6 refs.

Tissue obtained by biopsy from the liver of 2 children with von Gierke's (glycogen storage) disease and post mortem from that of 5 control subjects was homogenized and tested for glucose-6-phosphatase and phosphoglucomutase activity. The former enzyme is indispensable for the formation of sugar from glycogen or from non-carbohydrate precursors; its level in the liver tissue from the 2 cases of von Gierke's disease was found to be extremely low, being 1/12th of the lowest and 1/37th of the highest level found in the liver tissue from the controls. Phosphoglucomutase converts glucose-1-phosphate to glucose-6-phosphate and is essential both for the formation and breakdown of glycogen; its level in the cases of glycogen disease was found to be within the range of the values in the controls. The methods employed in analysis are described in detail.
L. H. Worth

Public Health and Industrial Medicine

1385. **Incidence of Dental Caries in Children under 5 Years Old**

G. L. SLACK. *British Medical Journal* [*Brit. med. J.*] 1, 260–263, Jan. 29, 1955. 1 fig., 19 refs.

Between 1948 and 1952 four different surveys were made of the dental condition of children under 5 years of age in Liverpool day nurseries, the object being to determine the incidence of caries and whether any variation in incidence occurred over a period of years. The children received three meals a day, supplemented by one pint (570 ml.) of milk, cod-liver oil, and orange juice; there were no between-meal snacks, but many of the children were given sweets or buns by their parents before and after attendance at the nursery. The numbers of children examined in each of the four years 1948–9 and 1951–2 were 324, 358, 594, and 633 respectively, a total of 1,909.

In 1952 the percentage of caries-free children was 90·6 in the second year of age, 66·8 in the third, 39·0 in the fourth, and 27·9 in the fifth and showed a similar age trend in the other years. There was a fall in 1949, followed by a rise in 1951 to a higher level than that observed in 1948, and the author discusses the possible relation between the observed incidence of caries and variations in the sweet ration. The average number of decayed, extracted, and filled teeth per child in 1952 was 0·2 in the second year of life, 1·8 in the third, 3·5 in the fourth, and 4·1 in the fifth. The high susceptibility to caries of the deciduous molars was striking, over 45% of the second molars being decayed before the age of 5 years.

The finding of an average of 5 decayed teeth in every school entrant is examined in relation to the capacity of a full-time school dentist to complete about 3,000 fillings a year. The author comes to the conclusion that the entire establishment of the school dental service of Liverpool would be insufficient to deal each year with this age group alone. He draws attention to two measures which are of proved value in reducing the incidence of caries—the fluoridation of domestic water supplies and the use of a mouth rinse of plain water after eating and drinking.

F. T. H. Wood

1386. **Medical Aspects of Excessive Fluoride in a Water Supply**

N. C. LEONE, M. B. SHIMKIN, F. A. ARNOLD, C. A. STEVENSON, E. R. ZIMMERMANN, P. B. GEISER, and J. E. LIEBERMAN. *Public Health Reports* [*Publ. Hlth Rep. (Wash.)*] 69, 925–936, Oct., 1954. 15 refs.

The authors report the results of a 10-year comparative study which was initiated in 1943 in an attempt to determine the effects of prolonged ingestion of fluoride in drinking water. It was carried out on 116 citizens of Bartlett and 121 of Cameron, two small towns in Texas comparable in most respects except that the water supply of Bartlett, derived from deep wells, had a fluoride content (until 1952) of 7·6 to 8·2 p.p.m. while in that of Cameron, taken from the local river, the content was only 0·4 to 0·5 p.p.m. All subjects selected for study in 1943 had been resident in one or other of the towns for at least 15 years; their ages at that time ranged from 15 to 68 years and the average duration of exposure of the Bartlett group to high fluoride concentration was 36·7 years. Full physical, laboratory, and radiological examinations were made and medical histories from birth taken of all subjects in 1943, and again in 1953, with the exception of 18 who had died and 10 who had gone away to distant parts of the country. Estimations were made of the degree and prevalence of dental fluorosis and of the incidence of caries, gingivitis, and alveolar bone loss, the dental radiographs being evaluated independently by four dentists. Information regarding the dead was obtained from next of kin and from death certificates, while all the 10 persons who had gone away were communicated with and reported no serious acute or chronic illness; thus all subjects seen in 1943 were accounted for in 1953.

As was not unexpected, dental fluorosis was observed in Bartlett in all the subjects born there and who had continuously resided there during the tooth formative period. There was one single case of dental fluorosis in the Cameron group, but investigation showed that this individual had a history of early exposure to fluoride. No new cases of dental fluorosis appeared among the subjects from either town during the 10-year period of the study. The only other finding of note was that cardiovascular abnormalities reached a significantly higher level in the subjects from Cameron. It is concluded that the investigation has shown that no clinically significant physiological or functional effects, other than dental fluorosis, have resulted from prolonged consumption of water with an excessive fluoride content.

J. Cauchi

1387. **Results of Whooping-cough Vaccination**

A. R. FOLEY. *Canadian Journal of Public Health* [*Canad. J. publ. Hlth*] 45, 392–395, Sept., 1954. 3 figs.

Writing from the Health Department of the Province of Quebec, the author discusses the results of whooping-cough vaccination in the Province since 1946, when a campaign to vaccinate the whole population was initiated. Vaccination with combined diphtheria-toxoid–pertussis vaccine consisted of 4 injections beginning at 3 months of age, the first dose being 0·5 ml.; the second and third doses, each of 1 ml., were given at monthly intervals, followed by the fourth dose of 0·5 ml. 3 to 12 months later. Additional vaccination was given when the child entered school or if an epidemic broke out.

Of an average number of 125,000 live children born annually, some 60% have been vaccinated—a proportion

which is considered too small. Nevertheless there has been a notable fall in the number of cases of whooping-cough notified. Thus before 1946 a widespread epidemic occurred every 3 years, with a morbidity of between 150 and 250 cases per 100,000. Since 1946 the interval between epidemics has been increased to 4 years and the highest peak of incidence has been of the same order as the lowest incidence in pre-vaccination years. The mortality figures have shown a closely similar trend.

A closer study was made of a sample of 327 cases of whooping-cough reported in 1953; of these, 160 children (48·9%) had not been vaccinated, 115 (35·2%) had been vaccinated, and in 52 cases (16·9%) the status of immunity was unknown. The effect of vaccination on mortality was, however, more striking; of 66 deaths occurring in 1953, 30 were of children under 6 months of age. In 61 of these cases it was established that there had been no vaccination at all, and in 3 cases vaccination had been only partial; the remaining 2 cases could not be traced. No deaths of fully vaccinated children were recorded. The author concludes that children who have been vaccinated may develop whooping-cough, but if they do they are not likely to die.

Benjamin Schwartz

1388. **Acute Aseptic Meningitis during an Influenza-like Epidemic in Greenland.** [In English]

E. DEIN. *Acta psychiatrica et neurologica Scandinavica* [*Acta psychiat. neurol. scand.*] **29**, 319–332, 1954. 3 figs., 21 refs.

In the autumn of 1951 there was an epidemic of a condition resembling influenza in the southernmost parts of West Greenland, during which a number of patients developed benign meningitis, of whom 47 came under observation, 79 lumbar punctures being performed on 35 of these patients. The victims were mostly children under the age of 12, of mixed European and Eskimo stock. The cell count in the cerebrospinal fluid varied, but was sometimes very high, the cells being predominantly mononuclear leucocytes. Various laboratory investigations were carried out whereby it was possible to exclude most of the known viruses with reasonable certainty.

Hugh Garland

1389. **An Outbreak of Food Poisoning due to *Salmonella typhi-murium* with Observations on the Duration of Infection**

M. LENNOX, R. W. S. HARVEY, and S. THOMSON. *Journal of Hygiene* [*J. Hyg. (Lond.)*] **52**, 311–314, Sept., 1954. 1 fig., 4 refs.

An outbreak of food poisoning due to *Salmonella typhimurium* in a school of 250 pupils, in which it was possible to observe the entire population at risk and the duration of infection, is described in detail.

A total of 64 children, all under the age of 10, had diarrhoea and abdominal pain, and infection was attributed to the school milk which was "tuberculin tested" but unpasteurized. Specimens of faeces from the affected children were examined twice weekly, beginning 2 weeks after the outbreak. Faecal specimens from the remaining 186 children who had no symptoms were examined 2 to 3 weeks after the onset; 24 of these children were found to be excreting *Salm. typhimurium*.

The authors discuss the duration of infection in infectious diseases. In the outbreak described in this paper the number of children excreting the organism fell slowly for 3 weeks, declining rapidly thereafter. This is clearly shown on a logarithmic chart, and the authors point out that the curve is similar to that obtained by others for paratyphoid fever. The rate of clearance in the 24 symptomless carriers was the same as that observed in those with symptoms.

A. Trevor Jones

INDUSTRIAL MEDICINE

1390. **Patch-testing Methods Applied to the Study of Cutaneous Hypersensitivity of Occupational Origin.** (La méthode des tests épicutanés, appliquée a l'étude des réactions d'intolérance cutanée d'origine professionnelle)

J. CHARPY, P. Y. CASTELAIN, and H. GÉRARD. *Archives des maladies professionnelles, de médecine du travail et de sécurité sociale* [*Arch. Mal. prof.*] **15**, 351–356, 1954.

In this paper the authors make a plea for the systematic and thorough patch-testing of all cases of skin sensitization. At the Dermatological Clinic of the Hôtel-Dieu, Paris, during the last 2 years some 15,000 tests have been performed in a systematic investigation of all patients suffering from eczema or skin sensitization, and especially of suspected cases of occupational dermatitis. From this it emerged that three types of reaction may be elicited: (1) the positive, specific reaction of sensitization; (2) the reaction of irritation, the result of the application of a strong irritant which, in a similar concentration, would not cause irritation in other individuals; (3) a reaction called by the authors a "collective effect," typically caused by certain soaps and shampoo agents which have a caustic action, and varying in degree from a roughening of the skin to blistering and even necrosis. This "collective effect" is capable of facilitating the penetration of the skin by other materials and so producing sensitivity—a fact of great importance.

Out of a recent series of 120 cases of suspected occupational skin disease 80 results were available. Examples of these are given, such as that of a mason afflicted with eczema of both hands, forearms, and face, which was diagnosed by his doctor as "occupational disease from cement". All tests with cements and with chrome, however, proved negative, and the systematic application of some 40 other tests gave only one positive result, that from the shaving cream which he daily applied with his hands to his face. On his discontinuing the use of this cream the eczema healed completely and the mason resumed his former work without any further skin trouble.

The authors point out that the development of a specific eczema may, in time, produce a poly-sensitization, so that a worker sensitized to cement, chrome, or a hair-dye may become sensitized also to shaving soap, brilliantine, dentrifice, textiles, rubber gloves, or other materials. Conversely, sensitivity may be extremely selective, as was

seen in the case of 2 electricians of whom one was sensitive only to a yellow-coloured and the other only to a black insulating material. Again, sensitization may be caused by contact with materials not used in the actual work process, such as detergents and abrasive soaps used for cleaning the hands after work.

Patch-testing can confirm or exclude the occupational nature of a skin sensitization. It can also designate: (1) the association of an occupational with a non-occupational causal agent; (2) the precise agent incriminated, which may necessitate a change of occupation, or the ban may be limited to a material which can be avoided; (3) the possible incrimination of a non-essential material which is used at work but which can be eliminated. The authors stress that there are cases of dermatitis which are clinically occupational in origin, but not so in a legal sense. In this connexion the problems of compensation are briefly discussed. Of the 80 cases reported, only 44 proved to be true cases of occupational disease. In the authors' opinion the diagnosis of occupational skin disease ought to be rejected unless accompanied by the evidence provided by standardized tests carried out by personnel with long experience in this type of work.

M. A. Dobbin Crawford

1391. **The Effects of Water and Salt Intake upon the Performance of Men Working in Hot and Humid Environments**

W. S. S. LADELL. *Journal of Physiology* [*J. Physiol. (Lond.)*] **127**, 11–46, Jan. 28, 1955. 10 figs., bibliography.

1392. **Treatment of Organic Lead (Tetraethyl) Intoxication with Edathamil Calcium–Disodium**

K. V. KITZMILLER, J. CHOLAK, and R. A. KEHOE. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg.*] **10**, 312–318, Oct., 1954.

This report from the University of Cincinnati College of Medicine describes the treatment of 3 cases of organic lead poisoning with the calcium disodium salt of ethylenediaminetetraacetic acid ("edathamil", EDTA). Organic lead poisoning is seen almost exclusively in workmen engaged in cleaning storage tanks for petrol containing tetraethyl lead, a sludge which forms at the bottom of the tank being the potential source of dangerous concentrations of lead in the atmosphere, making it possible to absorb a lethal dose of tetraethyl lead in half an hour's exposure. The symptoms are delayed in onset and ill-defined at first, but in the more serious cases the illness progresses rapidly towards a state of acute mental disturbance, with delirium, mania, convulsive seizures, and coma. Visual and auditory hallucinations are usually present. Lucid periods occur but relapses are common, so that prognosis as to life should be guarded during the early stages. In favourable cases recovery is complete within 4 to 10 weeks. Clinical and laboratory details are given of 2 cases of exposure to tetraethyl lead which were treated with EDTA alone, and of one treated with EDTA and dimercaprol (BAL), the daily dose of EDTA being 1 g. per 30 lb. (74 mg. per kg.) body weight, given intravenously for periods up to 8 days. Details of one case treated with BAL alone and of 2 in which general measures only were applied are included for comparison.

Although the authors admit that no valid conclusions on the therapeutic value of EDTA can be drawn from these cases, they claim that since the drug causes an increase in the excretion of lead it must reduce the severity and duration of the disease. No harmful effects of any kind were observed.

P. N. Magee

1393. **Inhalation Toxicity of Ninety Per Cent Hydrogen Peroxide Vapor. Acute, Subacute, and Chronic Exposures of Laboratory Animals**

F. W. OBERST, C. C. COMSTOCK, and E. B. HACKLEY. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg.*] **10**, 319–327, Oct., 1954. 15 refs.

In this paper from the U.S. Army Chemical Center attention is drawn to the increasing use of 90% hydrogen peroxide and to the small amount of information available in the literature concerning the toxicity and irritating effects of its vapour. Experiments are described in which the inhalation toxicity and irritant effect on the eye were studied in dogs, rabbits, rats, and mice under varying conditions. (The type of inhalation chamber and the methods used are fully described in the text.) Rats exposed for 8 hours to H_2O_2 vapour in concentrations varying from 243 to 307 p.p.m. showed no outward toxic signs apart from scratching and licking themselves, and none died. Congestion of the trachea and lungs with small localized areas of pulmonary oedema were found on pathological examination. Groups of rats and mice exposed to concentrations of H_2O_2 vapour varying from 57 to 77 p.p.m. for 6 hours a day, 5 days a week, for 6 weeks showed signs of extensive body irritation, with profuse nasal discharge and bleaching of the hair. More than 50% of the mice died after 8 exposures, but only one rat in 10 died after 30 exposures. Two dogs were similarly exposed to an average concentration of 7 p.p.m. and developed external body irritation, sneezing, lacrimation, and bleaching of the hair. Examination showed great thickening of the skin, but no destruction of hair follicles. The lung was the only internal organ to show any abnormality, and no significant changes were found in the blood or urine. Rabbits exposed for 3 months to a concentration of 20 p.p.m. developed no signs of eye injury.

The authors stress the importance of making direct determinations of the concentration of H_2O_2 vapour, having noted serious discrepancies between calculated and measured values. They conclude that if H_2O_2 vapour were to leak continuously into an area under conditions of poor ventilation the hazard would be serious, and state that the maximum allowable concentration of 90% H_2O_2 vapour is less than 7 p.p.m.

P. N. Magee

1394. **Focal Cerebral and Cerebellar Atrophy in a Human Subject Due to Organic Mercury Compounds**

D. HUNTER and D. S. RUSSELL. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **17**, 235–241, Nov., 1954. 9 figs., 9 refs.

Anaesthetics

1395. **Levorphan in Anaesthesia**
A. K. BROWN. *British Medical Journal* [*Brit. med. J.*] **2**, 967–969, Oct. 23, 1954. 2 refs.

The results are reported of an investigation into the merits of levorphan (" dromoran ") as a premedicating agent before general anaesthesia, in comparison with those of " omnopon ". Each of 100 patients was given 2 mg. of levorphan preoperatively, 20 of them receiving $\frac{1}{100}$ grain (0·65 mg.) of atropine, and 50 receiving $\frac{1}{150}$ grain (0·43 mg.) of scopolamine in addition. Another 50 patients received $\frac{1}{3}$ grain (22 mg.) of omnopon together with scopolamine in the above dosage. All the drugs were given by subcutaneous injection, the interval before induction varying from $\frac{1}{2}$ to 5 hours. Apprehension, drowsiness, amnesia, alteration in pulse rate, respiratory depression, and nausea were looked for and their presence or absence recorded in every case (the incidence of each in the various groups being presented in tabular form). It is concluded that levorphan has a definite sedative action, and that the effects of 2 mg. of this drug do not differ significantly from those of $\frac{1}{3}$ grain of omnopon, except that they last longer.

In another investigation levorphan was given as a continuous intravenous drip to supplement the effects of nitrous oxide and oxygen. It was found unsatisfactory for this purpose on account of the frequency with which it caused respiratory depression and the high incidence of postoperative respiratory complications.

Ronald Woolmer

1396. **Anaesthesia for Intra-nasal and Intra-oral Operations in Adults. Trial of a Technique Based on Intravenous Pethidine**
E. H. FRANKS. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **26**, 418–426, Nov., 1954. 2 figs., 20 refs.

1397. **Nisentil (1 : 3-Dimethyl-4-phenyl-4-propionoxypiperidine): a New Supplement for Nitrous Oxide–Oxygen–Thiopentone (Pentothal Sodium) Anaesthesia**
E. S. SIKER, F. F. FOLDES, NEUNG-MAN PAHK, and M. SWERDLOW. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **26**, 405–410, Nov., 1954. 1 fig., 27 refs.

The efficacy of " nisentil " (1:3-dimethyl-4-phenyl-4-propionoxypiperidine) was compared with that of pethidine, to which it is closely related, as a supplement to thiopentone–nitrous-oxide anaesthesia in 1,356 patients at the Mercy Hospital, Pittsburgh. The criteria used for the comparison were: (1) the dose of thiopentone, in mg. per minute, required to maintain adequate anaesthesia without undue depression of the respiratory rate; and (2) the percentage of patients responding to stimuli within 5 minutes of the end of the operation. The dose of thiopentone required with nisentil was smaller than that required with pethidine, and a larger percentage of patients reacted to stimuli at the end of the operation. Nisentil is a drug of shorter action than pethidine, and therefore allows greater flexibility of control; however, in large doses it causes considerable respiratory depression.

Ronald Woolmer

1398. **Hypotensive Spinal Anesthesia: Respiratory, Metabolic, Hepatic, Renal and Cerebral Effects**
N. M. GREENE, J. P. BUNKER, W. S. KERR, J. M. VON FELSINGER, J. W. KELLER, and H. K. BEECHER. *Annals of Surgery* [*Ann. Surg.*] **140**, 641–651, Nov., 1954. 1 fig., 41 refs.

In view of the increasing use of " hypotensive " spinal analgesia the authors have considered the question whether this procedure could cause transient or permanent organic damage as a result of the concomitant fall in cardiac output and reduced renal, hepatic, and cardiac blood flow by which it is accompanied. They have therefore investigated the renal, hepatic, and cerebral functions, pulmonary ventilation, blood concentration of cellular metabolites, and acid–base balance before, during, and after operation in patients receiving this type of analgesia at Massachusetts General Hospital.

Under anaesthesia induced with thiopentone and maintained with nitrous oxide and oxygen, total sympathetic block was performed by spinal injection of one of the usual blocking agents in hyperbaric solution. Of the 17 cases in which arterial oxygen content and saturation were estimated, only 3 showed a slight fall. The blood carbon dioxide tension, determined in 22 cases, showed a marked rise in only 2, while in 16 out of 22 cases there was a very slight disturbance in acid–base balance. No rise in the blood amino-acid nitrogen level occurred in any of the 17 cases investigated. Disturbances of hepatic function postoperatively were noted in all 29 cases studied, but the variations from normal were, on the whole, less than those occurring with usual anaesthetic techniques. Little alteration in renal blood flow or glomerular filtration rate was found in the 8 cases in which these functions were investigated. Indeed, the only disturbance of note was the finding of some evidence of mental impairment in 5 out of 25 patients subjected to a battery of psychomotor tests before and after operation. However, very similar results were obtained in a series of 13 normotensive patients undergoing the same tests.

The authors are well satisfied that hypotensive spinal analgesia compares favourably, in regard to the effects studied, with normal anaesthetic techniques—with the possible exception of cerebral function which, they suggest, requires fuller investigation.

[Full analytical details of the laboratory investigations are given in a number of tables, for which the interested reader should refer to the original paper.]

Michael Kerr

1399. Role of Antihistaminic Drugs in Regional and Spinal Analgesia

C. R. STEPHEN, W. K. NOWILL, H. HALL, R. MARTIN, and G. MARGOLIS. *Anesthesiology* [*Anesthesiology*] **15**, 601–622, Nov., 1954. 5 figs., 16 refs.

It is known that some antihistaminic drugs have specific effects on certain tissues or organ systems; for example, tripelennamine hydrochloride ("pyribenzamine") has been shown to exhibit anaesthetic activity when applied to mucous membranes in low concentration, and further examples are cited from the literature. In view of these reports the authors, working at Duke University School of Medicine and Hospital, Durham, North Carolina, have investigated the local analgesic properties of pyribenzamine, "antistin" (antazoline), and methapyrilene hydrochloride in the rabbit and in a number of patients. Regional and subarachnoid injections of the three drugs were given, the effect and duration of action noted and compared with those of procaine, and the injected nerves and spinal cords of the rabbits removed and examined histologically.

Tripelennamine, compared with procaine, caused very slightly longer but less profound regional analgesia. Using Sunderland's classification of nerve injury, it was estimated that 1 and 2% solutions of tripelennamine produced second-degree injuries in 3 out of 38 nerves, and 5% solutions produced such injury in 5 out of 8 nerves. Both the other drugs caused severe nerve injury, in some cases in concentrations as low as 1%. Comparable changes caused by 1% procaine were minimal, and an increase of its concentration to 5% did not increase its toxic effect. Perineural injuries were also much greater with the antihistaminics. Further, tripelennamine in doses totalling 10 mg. per kg. body weight was strongly convulsant, producing convulsions and death in rabbits. In spinal analgesia the depression of motor and sensory function was less pronounced with tripelennamine than with procaine; all the animals tested appeared to make a complete functional recovery.

Skin-weal tests of tripelennamine were conducted on human volunteer subjects; in these the analgesia tended to be longer than that produced by procaine, but the stronger solutions were painful and caused necrosis and sloughing of the skin. Regional nerve blocks, performed in 35 cases, were more effective, more profound, and lasted somewhat longer than those obtained with procaine. The drug was given 100 times as a spinal analgesic to 67 poor-risk patients. No profound or disturbing hypotension was noticed. In 14 of 30 cases in which the cerebrospinal fluid was examined later there were no abnormalities; a positive Pandy reaction was noted in 8 samples, and an increased lymphocyte count also in 8.

The authors conclude that it is doubtful whether these agents are as safe or as effective as procaine. They may cause severe injury to nervous tissue and their therapeutic–toxicity ratio is lower. Clinical studies tend to give a misleadingly optimistic impression which is not confirmed by animal studies. Examination of the analgesic properties of other antihistaminics, however, is advocated.

W. Stanley Sykes

1400. Long-term Follow-up of Patients Who Received 10,098 Spinal Anesthetics

R. D. DRIPPS and L. D. VANDAM. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **156**, 1486–1491, Dec. 18, 1954. 13 refs.

Spinal analgesia was administered on 10,098 occasions to 8,460 patients over a 4-year period at the Hospital of the University of Pennsylvania, Philadelphia, by a technique which is described here in detail and with a variety of drugs and combinations of drugs. At the same time a series of 1,000 patients received general anaesthesia for operations of a similar nature, and an additional 75 patients received spinal analgesia while under general anaesthesia and never knew that they had had a spinal injection. The patients were watched carefully for any early neurological sequelae while they were still in hospital and received a questionary 6 months after discharge which gave them ample opportunity to complain of any symptom which they might themselves have attributed to the analgesia. In view of the current distrust of spinal analgesia in both the medical and lay mind the incidence of sequelae as revealed by this method of study might be expected to be unusually high, but in fact not a single major neurological disability was discovered which was directly attributable to the analgesia; the only case of incapacitating neurological disease was due to a meningioma which had been present at the time of analgesia, but had not given rise to symptoms until then. Headache occurred in 14% of cases in the main series, and it is notable that the same proportion of the 75 patients who did not know they had had spinal analgesia also complained of headache. Eight instances of transient sixth-nerve palsy occurred, all associated with the use of a wide-bore (16-gauge) needle. In 66 instances there were complaints of paraesthesiae of the limbs or perineum, disappearing within a year of the operation. Backache with pain radiating to the legs occurred in 4 cases in which the lumbar puncture had caused trauma, but in 2 of these no analgesic had been injected intrathecally so that it appeared to be the puncture itself that was culpable. In 9 cases in which pre-existing neurological disease had not been recognized preoperatively an exacerbation of the condition occurred after spinal analgesia.

The conclusion drawn by the authors from this study is that the pendulum of prejudice against spinal analgesia has swung so far that some patients for whom spinal analgesia is the method of choice may well be denied it unnecessarily. The widely-held belief that incapacitating complications are common has obscured the fact that the mortality attributable to its use is less than for general anaesthesia.

[It would seem fair to comment that in expert hands in a first-class institution spinal analgesia carries very little risk. Where personal skill or theatre facilities are anything less than excellent, general anaesthesia is probably safer as regards non-fatal sequelae.]

Donald V. Bateman

1401. The Anesthetic Properties of Cyclobutane

L. D. VANDAM and R. D. DRIPPS. *Anesthesiology* [*Anesthesiology*] **16**, 48–56, Jan., 1955. 1 fig., 11 refs.

Radiology

1402. Risks from Chronic Irradiation and Their Haematological Control

R. H. MOLE. *Journal of Clinical Pathology* [*J. clin. Path.*] 7, 267–274, Nov., 1954. 9 figs., 30 refs.

In this paper from the Medical Research Council's Radiological Research Unit, Harwell, the literature from 1914 to the present day on the haematological effects of irradiation is critically surveyed.

In experiments on mice, dogs, and guinea-pigs irradiated with 20 to 80 times the maximum permissible dose (m.p.d.) for human beings the blood lymphocyte count fell during the first few months and then remained constant at the lower level, whereas the neutrophil leucocyte count fell to a lesser degree. No progressive fall in the blood cell count preceded death in the guinea-pigs; in a monkey dying after ingestion of radioactive strontium the leucocyte count was normal on the day of death, but the animal suddenly developed anaemia as a result of a steady fall in the haemoglobin level and in the erythrocyte count. Similar observations have been made in human subjects with aplastic anaemia due to irradiation.

There is considerable variation in the leucocyte count in all human subjects, especially when ordinary working conditions are poor, but the lymphocytes are least affected in the differential count. Some authors have reported marked skin changes without any change in the blood count in subjects exposed to irradiation. Animal experiments and experience with human beings show that exposure to radiation at levels above 20 m.p.d. results in a small fall in the granulocyte or lymphocyte count, or both, but such overdosage should not occur where there is proper physical control.

The author questions whether the peripheral circulation reflects the state of the haematopoietic tissue. The gonads are more sensitive to irradiation than the blood count, although damage to them is less easily assessed. In his view the greater sensitivity of the gonads is at least one reason why radiation hazards "should be measured physically rather than by controlled laboratory examination of the exposed individual". He concludes that the blood count is of little value as an indication of damage from irradiation. *G. E. Flatman*

1403. Pituitary and Orbital Roentgen Therapy in the Hyperophthalmopathic Type of Graves' Disease. [In English]

O. GEDDA and M. LINDGREN. *Acta radiologica* [*Acta radiol. (Stockh.)*] **42**, 211–220, Sept., 1954. 2 figs., 27 refs.

In addition to the appropriate medical treatment, 19 patients with the hyperophthalmopathic type of Graves's disease received *x* irradiation at the University Hospital, Lund, Sweden. Radiotherapy was directed to the pituitary region in 16 cases and to the orbits only in 3. The pituitary region was irradiated (170 kV, H.V.L. 0·9 mm. Cu) in two series of treatments at an interval of about 5 weeks; four temporal fields were used, each of which received 1,500 r in the first series and 600 to 900 r in the second series; a suitable depth dose for the hypophysial region appeared to be 3,000 to 4,000 r in 60 to 90 days, or the corresponding dose in relation to the time factors. From condenser-chamber dose measurements it was found that the posterior part of the orbits received roughly the same dose as the pituitary region; it was possible, therefore, that regression of the eye disturbances was due, at least in part, to the direct irradiation of orbital tissue. For orbital irradiation lateral fields were used, treatment being given in two series at an interval of 4 to 5 weeks; the daily skin dose was 100 to 150 r, the total skin dose per field being 900 r in the first series and 600 to 900 r in the second.

Of the 16 patients in the first group, the effect was good in 10, as judged by the disappearance of lacrimation, photophobia, and ophthalmoplegia. The remaining 6 patients subsequently received additional irradiation of the anterior part of the orbits, and in 4 cases this was followed by disappearance of eye symptoms. Ten of the 16 patients originally had symptoms of hyperthyroidism; these disappeared after treatment and all 10 gained weight. In 2 of the 3 cases treated by irradiation of the orbits only, the result was highly satisfactory, but the treatment had no effect on the third case, which was of 5½ years' duration.

Satisfactory regression of the eye symptoms was thus obtained in most of these patients. While some of the improvement was evidently attributable to direct orbital irradiation, irradiation of the pituitary region was effective in suppressing the increased thyrotrophic activity of the gland in all 10 hyperthyroid cases. The authors conclude that differences in the results reported by various workers may be explained by differences in the stage at which treatment was given, it being important to start irradiation of the hyperfunctioning organ, the pituitary gland, as soon as possible. *Arthur Jones*

1404. The Use of Endobronchial Radioactive Cobalt. (Die endobronchiale Radiokobalt-Anwendung)

K. P. FISCHER. *Strahlentherapie* [*Strahlentherapie*] **94**, 374–383, 1954. 5 figs., 9 refs.

An intracavitary technique for the irradiation of centrally located bronchial carcinomata is described, in which "pearls" of radioactive cobalt threaded on a steel wire are employed. Each pearl is 6 mm. in diameter and is coated with gold to absorb the beta rays, its initial activity being 5 to 6 mc. Light general narcosis for 8 hours is necessary to suppress the cough reflex. A string of 10 pearls will give a maximum surface dose of 550 r per hour; in 8 hours this gives 4,400 r

maximum, 2,400 r at 1 cm. depth and 600 r at 3 cm. depth. The procedure is very well tolerated, even by patients in poor condition, as the general radiation effects are negligible. It is particularly suitable for supplementing external irradiation and to provide rapid relief of symptoms in cases of pulmonary collapse. So far, experience of the method has been limited to 6 patients treated in 6 months at the Darmstadt Roentgen Institute.

J. Walter

1405. **A Cobalt 60 Beam Unit with a Source–Skin Distance of 20 cm.**

F. W. SPIERS and M. T. MORRISON. *British Journal of Radiology* [*Brit. J. Radiol.*] **28**, 2–7, Jan., 1955. 10 figs., 7 refs.

1406. **Percutaneous Vertebral Angiography**

P. NAMIN. *Journal of Neurosurgery* [*J. Neurosurg.*] **11**, 442–457, Sept., 1954. 11 figs., 9 refs.

The changes in form and situation of the vertebral artery and its branches caused by the presence of space-occupying lesions in the posterior fossa of the skull are discussed with reference to 162 such cases in which vertebral arteriography was performed at the Hôpital de la Pitié, Paris. Puncture of the vertebral artery at the base of the skull with the patient lying prone was found to give more consistently successful results than the more usual anterolateral approach between two transverse processes with the patient lying supine. Continuous injection of saline between films was not used, an obturator being inserted into the needle instead. Usually 3 lateral exposures were made at one-second intervals and 3 in the anteroposterior projection with a 35-degree tilt of the tube and the same timing. If the patient was prone the same tube tilt was used. Very occasionally the full axial projection was employed.

Details of the anatomy of the basilar artery and its branches, as demonstrated by injection with plastic material followed by destruction of the brain tissue, are then given and related to the arteriographic appearances. The lateral view shows that the basilar trunk, which is the continuation of the vertebral artery injected, makes three distinct curves, the concavity being successively posterior, anterior, and posterior, with a clear space lying posterior to the clivus. The inferior cerebellar arteries, though always present, are very variable in size and may arise from the basilar or the vertebral arteries. The origins of the superior cerebellar arteries from the basilar trunk are remarkably constant and symmetrical; their course round the cerebral peduncles is clearly seen in the angiogram running parallel to that of the posterior cerebral arteries, which are visible throughout together with their temporal and occipital branches. The author claims that the lateral arteriogram gives information concerning: (1) the brain stem and the interpeduncular cisterns; (2) the situation of the pineal body and the corpora quadrigemina; (3) the state of the roof of the third ventricle; and (4) the cuneus of the occipital lobe. In the anteroposterior arteriogram the most important landmark is the division of the basilar artery in the midline. The whole course of the posterior cerebral arteries curving round the cerebral peduncles is seen, and the temporal and occipital branches are well visualized. The full axial view is used only to show vascular malformations of the basilar trunk and of its collateral branches. The findings in 9 cases of lesions in the posterior fossa are described; these included intracerebral and extracerebral tumours and arterial thromboses.

The author does not consider vertebral arteriography to be a dangerous procedure; in this series of 162 investigations there were 4 serious accidents, 2 of which were fatal. The contraindications include hypertension, renal failure, and diffuse arteriosclerosis with coronary disease.

W. B. D. Maile

1407. **The Roentgenological and Pathological Aspects of Tuberculosis of the Skull**

J. P. TIRONA. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **72**, 762–768, Nov., 1954. 4 figs., 5 refs.

1408. **Pneumotomography.** (La pneumostratigraphie)

G. GIRAUD, P. BÉTOULIÈRES, H. LATOUR, and M. PÉLISSIER. *Presse médicale* [*Presse méd.*] **62**, 1781–1785, Dec. 25, 1954. 12 figs.

The technique of pneumotomography (or pneumostratigraphy) is of particular value in the investigation of mediastinal structures. Either air filtered through cotton wool or oxygen can be used; the former is absorbed more slowly and should be used if the tomograms cannot be taken within a few hours of injection. The precoccygeal route of injection is the most usual, 500 to 800 ml. being injected in not less than 15 to 20 minutes. Various other possible routes are enumerated. Tomograms may be taken up to 48 hours after the injection of air, preferably after 10 to 12 hours, when contrast and diffusion will be at their maximum; cuts may be made in any plane, and the normal appearances in some of these are detailed. The examination is of secondary interest in determining cardiac pathology, but may be of great help in the diagnosis of lesions of the oesophagus, aorta, and pulmonary vessels, and in investigating mediastinal tumours.

Below the diaphragm the retroperitoneal space is less well defined, making demonstration of the organs by pneumotomography less satisfactory. The injection is again made by the precoccygeal route, 800 to 1,200 ml. of gas being injected rapidly. Gastric distension by the repeated administration of small quantities of an effervescent mixture is nearly always necessary. The exposures should be made with the patient in the upright position. The examination is of great help in cases of renal tumour, as well as adrenal tumour, hyperplasia, and calcification. It may also be of help in demonstrating splenic cysts and haematomata, and in the investigation of gastric disease. Pathological conditions of the inferior vena cava are rarely demonstrated, but enlargement of lymph nodes can be well visualized. Atheromatous plaques in the aorta may be demonstrated, and also certain lesions of the pancreas and liver.

John H. L. Conway-Hughes

History of Medicine

1409. **How Chemicals Entered the Official Pharmacopoeias.** [In English]
G. URDANG. *Archives internationales d'histoire des sciences* [*Arch. int. Hist. Sci.*] 7, 303–314, July–Dec., 1954. 7 refs.

The internal use of chemical drugs was a matter of bitter controversy between the orthodox and Paracelsian schools of medicine during the 16th and early 17th centuries, and the introduction of these drugs into official pharmacopoeias was the first authoritative recognition of modern therapy. The term " chemical " as used then implied a different meaning from that of today, embracing as it did not only inorganic chemicals, but also the " essential " forms obtained from crude drugs by chemical processes, such as distillation and crystallization. Aromatic waters, tinctures, and extracts, now classed with galenicals, were thus included in the concept " chemical ". The first official pharmacopoeia, that of Florence of 1498, as well as the 16th century pharmacopoeias of Nuremberg, Augsburg, and Cologne, strictly excluded the chemical remedies of Paracelsus. The Augsburg *Enchiridion sive dispensatorium* of 1564 listed a number of chemical preparations for external use, but these were known before the time of Paracelsus, and all the new compounds for internal use which were the subject of controversy were omitted.

In 1585 the Royal College of Physicians of London first planned the issue of a pharmacopoeia, and in 1589 established a Pharmacopoeia Committee, of which more than a third of the members had been educated abroad at the more liberal medical schools. It is therefore not surprising that the proposed contents of the pharmacopoeia included a group of substances under the title " Sales, chemica, metallica ", the very subjects of the Galenico-iatrochemical controversy. Unfortunately the whole project fell through, and the nature and intended use of these chemicals remain a secret.

The influence of the Paracelsian school, however, increased rapidly in the early years of the 17th century, owing largely to the work of Joseph Du Chesne and Oswald Croll, and in 1613 chemical drugs received their first official recognition in the 6th issue of the *Pharmacopoeia Augustana* edited by Raymond Minderer (1570–1621). The whole range of controversial remedies were included, and their use backed by decree of the Senate of Augsburg. The London *Pharmacopoeia* of 1618 was therefore not revolutionary when it also recognized chemical therapy, but was important in that its authority, by law, applied to a whole country, rather than only to a city republic as the Continental pharmacopoeias had done. It also supplied the actual formulae, instead of mere references to their authors, and listed three entirely new chemicals, tartarus vitriolatus, mercurius vitae, and mercurius dulcis (calomel). The chemical section was undoubtedly the work of Sir Theodore de Mayerne (1573–1655), a medical graduate of Montpellier and a Protestant refugee in England, who is shown to have owed much to Oswald Croll. Mayerne took pains not to provoke his opponents, and the now all-important chemical drugs made an unobtrusive entry into officially recognized therapy in England. *F. M. Sutherland*

1410. **Hospital Diets in Eighteenth Century England**
W. B. RABENN. *Journal of the American Dietetic Association* [*J. Amer. diet. Ass.*] 30, 1216–1221, Dec., 1954. 28 refs.

The author emphasizes that in Britain in the eighteenth century economy in administration was the first concern of hospital governors, since they were entirely dependent on public subscriptions for funds. This, together with the frequent issue of manuals on hospital practice, resulted in a general similarity of diets in hospitals in widely separated areas. Many provincial hospitals—at any rate in the earliest days of their existence—adopted diets based upon those provided at the London hospitals, although in the latter half of the century they offered a more generous diet than could be obtained in the metropolitan area.

By modern standards all the diets were nutritionally poor and unpalatable, and during the early period of the voluntary hospital movement there was only one bill of fare—variably known in different localities as the general, full, common, or ordinary diet—the basic items of which were broth, boiled beef or mutton, bread, and water gruel. Patients rarely received milk, the beverage usually given being weak beer. Soon, however, a " middle or half " diet was introduced to avoid waste by those patients who were unable to take the full allowance. Clinical experience also demonstrated the need for greater variation in the diet in the treatment of different diseases, and in the latter part of the century special diets were introduced; for instance, for patients with fever, pap, panada, and water gruel were prescribed because they were simple and easy to prepare, well-tolerated, and inexpensive.

Milk was gradually accepted as a useful food, especially for patients convalescent from fever. A dry diet, consisting of butter, cheese, bread, boiled beef or mutton, and a rice or a baked pudding, with restricted fluid intake, was prescribed for patients with oedema and ascites. Unfortunately a good deal of salt was used in the preparation of this dry diet, with the result that it was not as beneficial as it was expected to be, although fluid intake was restricted to one pint (568 ml.) of beer or cider daily. Mercury was widely prescribed, and special " salivating " diets were therefore given to patients receiving this drug; milk, broth, and beer were the staple nutrients, no solid food being allowed. Fish, fruit, and vegetables were rarely included in hospital diets, but some institutions—notably the Haslar Hospital

and the Edinburgh Royal Infirmary—adopted a more liberal attitude and included these items in the diet. Tea and coffee were seldom given because they were expensive and were regarded as bad for the sick. While beer formed the staple drink for the patients, most hospitals provided porter, ale, and gin for the staff.

Patients frequently complained about the diets, but these protests were met either with stony indifference or by dietary restriction which was imposed as a disciplinary measure. The impetus for the reform of hospital diets arose out of the recognition that the care of the sick remains ineffectual until nutrition is conducive to recovery. The general acceptance of this view in the nineteenth century led to the widespread revision of hospital diets. *H. P. Tait*

1411. **Giovanni Battista Monteggia (1762–1815), Physician to the Ospedale Maggiore of Milan, as the Author of the First Description of Infantile Paralysis (Acute Anterior Poliomyelitis).** (Giovanni Battista Monteggia (1762–1815) illustre médecin de l'Hôpital " Maggiore " de Milan, est le premier descripteur de la paralysie infantile (poliomyélite antérieure aiguë))
S. PICCINI. *Archives internationales d'histoire des sciences* [*Arch. int. Hist. Sci.*] **7**, 298–302, July–Dec., 1954. 2 figs., 10 refs.

In this contribution from the University of Milan the author points out some errors of omission in the third volume of Laignel-Lavastine's *Histoire générale de la Médecine*, notably of the names of Bassi, a forerunner of Pasteur who identified the causal organism in a disease of the silkworm, and of Bassini, who introduced an improved operative technique in the treatment of inguinal hernia. Chiefly, however, the author regrets the omission of the name of Giovanni Battista Monteggia, one of the foremost Italian physicians of the late 18th and early 19th centuries, who made a number of original contributions to medicine, and in particular, the author claims, gave the first clinical description of poliomyelitis. In support of this the Italian text (in facsimile) and a French translation are provided of the relevant section of Monteggia's *Istituzioni chirurgiche*, published in Milan in 1813. Monteggia has been largely ignored in historical accounts of infantile paralysis, and this the author attributes to the vast and general nature of the *Istituzioni*, in which the description of poliomyelitis is easily overlooked.

The first description of the disease has usually been credited to the 18th century English paediatrician, Michael Underwood; it appeared in the second edition of his *Treatise on the diseases of children*, published in 1789. Underwood, however, did not entirely distinguish poliomyelitis from general " scrofulous " paralysis, and failed to establish it as a clinical entity. This point is well brought out in the present article [but the case for Monteggia is not consolidated, as no bibliographical details are given of a previous article by the author in which the descriptions by Underwood and Monteggia are compared].

[The claims of Underwood to priority have been disputed, not only on behalf of Monteggia, but also on behalf of Johann Christoph Gottfried Joerg (1779–1856) of Leipzig. *A bibliography of infantile paralysis, 1789–1944*, published in Philadelphia in 1946, records the description of a case of poliomyelitis by Joerg in 1810, that is, three years before that claimed for Monteggia.] *F. M. Sutherland*

1412. **Anton Chekhov. General Practitioner and Pioneer in Social Medicine**
J. TODD. *Practitioner* [*Practitioner*] **173**, 605–610, Nov., 1954. 1 fig., 1 ref.

Anton Chekhov, born at Taganrog in South Russia in 1860 of lower middle-class stock, received his medical degree from Moscow University in 1884. As a student he had supported himself by " hack " writing, and although his future fame was to rest on his literary talent, he did not allow his literary triumphs to interfere with his medical career.

He practised first in Moscow and then in the country, about 50 miles away, at Melikhovo, where he was elected to the local Sanitary Council and given sole charge of the anticholera precautions. Quotations from letters written during this period depict a physician vividly interested in his professional career, which he valued as complementary to his career as a writer. Chekhov suffered from tuberculosis, and it was increasing ill-health which compelled him to abandon gradually the life of an active doctor. In 1890 " a sense of guilt " over his inability to practise regularly as a doctor induced him to undertake an arduous journey to the penal settlement on Saghalien Island. His description of the living conditions of convicts, which was a contribution to sociology, created such a sensation that officialdom was stirred into action. In the closing years of his life, when illness drove him to the resorts of the Crimea, the Riviera, and Germany, Chekhov maintained his contact with the medical world, raising money for hospitals and using his influence to save the *Chronicle of Surgery* from financial extinction. Many of Chekhov's characters were doctors—sometimes figures of fun—but Chekhov was quick to defend his profession against the bitter attacks of Tolstoy. His early death in 1904 was a loss both to Russian medicine and to the world of letters. *F. M. Sutherland*

1413. **A Note on John Hunter**
J. DOBSON. *Annals of the Royal College of Surgeons of England* [*Ann. roy. Coll. Surg. Engl.*] **15**, 345–346, Nov., 1954.

1414. **Alphonse Allais and Medicine.** (Alphonse Allais et la médecine)
R. CHAUVELOT. *Presse médicale* [*Presse méd.*] **62**, 1507–1511, Nov. 3, 1954. 2 figs.

1415. **Albrecht von Graefe: the Man in his Time. Part I**
E. V. ULLMAN. *American Journal of Ophthalmology* [*Amer. J. Ophthal.*] **38**, 525–543, Oct., 1954. 4 figs.

1416. **William Mackenzie, the Making of an Ophthalmologist**
J. MARSHALL. *Glasgow Medical Journal* [*Glasg. med. J.*] **35**, 258–270, Oct., 1954. 15 refs.